INDEX NUMBER

Vol. 6 JUNE, 1935 No. 6

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JUN 3 1935

THE JOURNAL OF PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

Official Organ for

THE AMERICAN ACADEMY OF PEDIATRICS

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The Journal of Pediatrics

VOL. 6 JUNE, 1935 NO. 6

Original Communications

WHOOPING COUGH

II. EXPERIMENTAL STUDY

CHARLES S. CULOTTA, M.D., DANIEL F. HARVEY, M.D., AND ERNEST F. GORDON, M.D.
NEW HAVEN, CONN.

THE rôle that the bacillus of Bordet and Gengou plays in the etiology of whooping cough is still disputed. Current opinion seems to be divided between those who favor the pertussis bacillus as the sole specific cause and others who believe that a filtrable virus acts at least as a necessary predisposing agent. Investigations on both apects of the problem are being presented in this paper.

PART I

The mass of evidence at hand shows that the Bordet-Gengou organism bears an important relationship to the disease. First, the presence of *H. pertussis* in a relatively high percentage of whooping cough patients early in the disease has been definitely established by many observers by the use of the cough plate method for early diagnosis (Chievitz and Meyer,[1] Lawson and Mueller,[2] Sauer and Hambrecht,[3] Gardner and Leslie,[4] Culotta and Harvey,[5] and others). The gradual disappearance of the Bordet-Gengou bacillus goes hand in hand with the decline in infectivity. Second, the organism is distinct from other species of bacteria and is absent in other catarrhal infections. Third, the appearance of complement-fixing bodies for *H. pertussis* during convalescence from whooping cough has been demonstrated. Fourth, *H. pertussis* has been recovered from the lungs of children who died of pneumonia complicating whooping cough (Smith,[6] also Fontayne[7]). Fifth, the results of experimental infection, although contradictory, merit serious consideration. The early claims to the suc-

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cessful implantation of *H. pertussis* in laboratory animals are open to serious criticism since methods were not available at that time for differentiating the pertussis bacillus from the distemper bacillus. (This is undoubtedly the basis for the contradictory reports in experimental whooping cough investigations.) More recent claims to the experimental transmission of the disease to animals are highly suggestive. Sauer and Hambrecht[8] reported the production of a characteristic paroxysmal cough in eight out of twenty-eight monkeys (a total of seventy-six tests) inoculated with *H. pertussis*. The cough was accompanied by a moderate lymphocytosis, and *H. pertussis* was recovered from deep throat cultures. These animals were found to be refractory to subsequent inoculations of *H. pertussis*, but unfortunately no mention is made of controls. More recently, Rich, Long, Brown, Bliss, and Holt[9] reported the production of a pertussis-like affection in a chimpanzee following inoculation with unfiltered sputum from a human case of pertussis and in two other chimpanzees following inoculation with suspensions of freshly isolated Bordet-Gengou bacilli. Mild catarrhal affections simulating colds were also observed in the two apes inoculated with unfiltered sputum. These authors state that "there can be no doubt that the three apes inoculated with pure cultures of Bordet bacilli or whole sputum developed typical whooping cough, which in its clinical and bacteriologic aspects was indistinguishable from the human disease." Shibley[10] has also reported transmission of whooping cough to apes following inoculation with *H. pertussis*. MacDonald and MacDonald[11] have reported the transmission of whooping cough to two children by intranasal instillation of *H. pertussis*.

It is apparent from the preceding considerations that legitimate claims to the successful experimental implantation of the *H. pertussis* are not very numerous; it is desirable to know more about the infectivity of laboratory animals to the organism in question. Therefore, we are reporting the results of our investigations in this field.

METHODS

The procedure used in the preliminary experiments consisted in the intratracheal inoculation of monkeys with saline suspensions of *H. pertussis*. Only strains recently isolated from cases of whooping cough were used (first to third generation cultures isolated from a cough plate). The culture medium used was essentially the Danish modification of the original Bordet-Gengou medium as recommended by Gardner and Leslie,[12] but human citrated blood (20 per cent) was substituted for horse blood. From forty-eight- to seventy-two-hour surface growths on three 15 cm. Petri dishes were suspended in 10 c.c. of physiologic sodium chloride solution, and from 2 to 4 c.c. of the suspension was injected in the monkeys. The virulence of the organism for white mice was determined by intraperitoneal inoculation, from 0.2 to 0.5 c.c. of this suspension being in all strains used the lethal dose (Sauer and Hambrecht[8]). The organism was readily recovered from the peritoneal cavity and heart's blood. All fresh strains were agglutinated by Gardner and Leslie's[12] Phase I antiserum in dilutions ranging from $\frac{1}{1000}$ to $\frac{1}{2000}$.

The monkeys used in the early experiments were of the Erythrocebus variety or the so-called "military" monkey. The *Macacus rhesus* was used subsequently because the monkeys of the former species were not available. The animals were under preliminary observation for a period of a week to two months. Frequent deep nose cultures were obtained to determine the normal bacterial flora. Distemper bacilli were not observed in these animals. Daily temperature readings and white blood counts were taken, and the animals were weighed at intervals. The intratracheal route was used with the monkey strapped on the operating board and head fully extended. An anesthetic usually was not necessary, but it is probably desirable.

EXPERIMENTAL

1. *Intratracheal Injection of H. Pertussis.*—The intratracheal route of infection was chosen because a heavy inoculation of the respiratory tract can be effected in

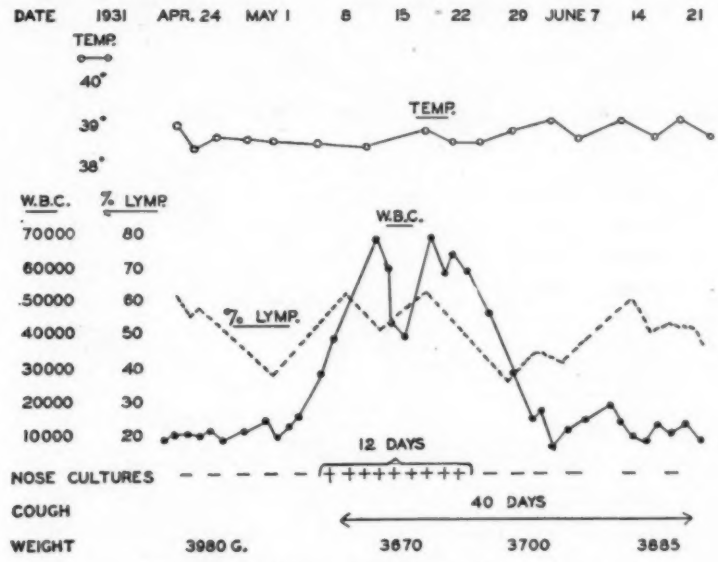

Chart 1.—Experiment 1. Experimental pertussis.

this manner. Three monkeys, two of the Erythrocebus variety and one *Macacus rhesus* developed a pertussis-like syndrome as is shown in the following protocols:

EXPERIMENT 1. (Chart 1.) Monkey 5, Erythrocebus, female, weighing 3,980 gm., May 1, 1931, was given an intratracheal injection of 4 c.c. of a saline suspension of virulent *H. pertussis* (Lawrence strain), which was prepared by washing off one plate of a seventy-two-hour culture (on Bordet-Gengou medium) in 10 c.c. of saline. The monkey remained well until May 8, the eighth day, when a cough developed and the leucocyte count began to rise with a corresponding increase in the lymphocytes. Deep nasal cultures remained negative for *H. pertussis* from the time of inoculation until May 8 just before the onset of the cough. Cultures were positive for twelve days, this period being not unlike the catarrhal stage clinically. The cough became more spasmodic, and vomiting occasionally occurred. The total duration of the cough was forty days. The white blood count reached its maximum at the

height of the cough, the highest reading being above 70,000 per cubic millimeter, the average count prior to inoculation was 15,000 per cubic millimeter. Signs of a diffuse bronchitis (râles, both bases posteriorly) were noted during this period. A roentgenogram of the chest showed an area of increased density in the left lower lobe. The lymphocytic response did not exceed 60 per cent, the base line during the preliminary period of observation being approximately 45 per cent. The temperature curve remained within normal limits. The animal lost weight but regained it during convalescence. This monkey has been under observation for a period of two years and has been well. No cough followed two subsequent similar attempts at reinfection to test immunity, but no conclusions as to immunity can be drawn since the control animals *(Macacus rhesus)* were also refractory.

EXPERIMENT 2. (Chart 2.) Monkey 2, Erythrocebus, male, weighing 3,020 gm., May 1, 1931, was given an intratracheal injection of 4 c.c. of the same saline sus-

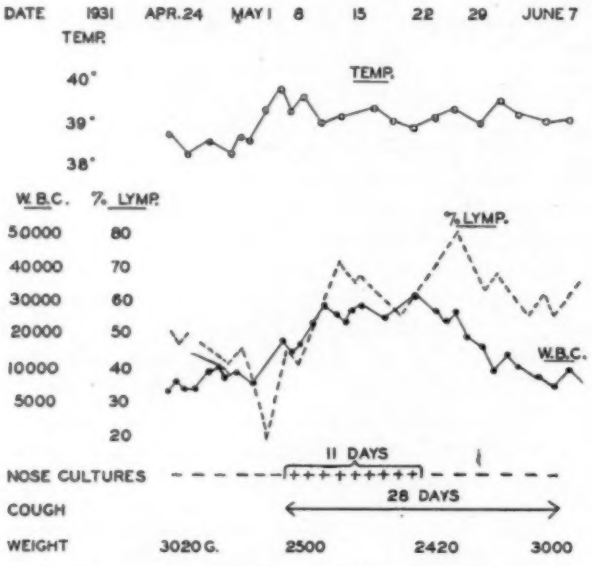

Chart 2.—Experiment 2. Experimental pertussis.

pension of Lawrence strain as in Experiment 1. Daily deep nose cultures were negative for *H. pertussis* until ninth day when organism was recovered. The nose cultures were positive for eleven consecutive days. The cough began on the tenth day, May 10, and coincidently there was a gradual rise in the white count with a definite lymphocytic response. The cough became progressively worse and more frequent, from three to four attacks occurring at times within one-half hour. The total duration of the cough was twenty-eight days. The white count reached its peak on the twentieth day, being 32,000 per centimeter, the average count prior to inoculation having been 8,000 per cubic millimeter. The lymphocytic response exceeded 75 per cent. There was only slight febrile reaction during the course. A loss of weight occurred as in Monkey 5, but a gradual gain occurred during convalescence. This animal remained well for a period of five months after this experiment and then developed a spontaneous, Group IV, pneumococcus pneumonia with meningitis. There were no signs of tuberculosis noted at postmortem examination.

EXPERIMENT 3. (Chart 3.) Monkey 77, *Macacus rhesus*, female, weighing 3,550 gm., March 28, 1932, was given an intratracheal injection of 5 c.c. of a saline suspension of virulent *H. pertussis*, four different strains being used. The suspension was prepared as in Experiment 1. The monkey began to cough on the eighth day and continued to cough for thirty-six days. The deep nose cultures were positive for *H. pertussis* for a period of twelve days. The white count gradually rose to above 50,000 per cubic millimeter, the base line prior to inoculation being 20,000 white blood cells per cubic millimeter. The lymphocytic response in this animal was not as striking as in the previous experiments. The lymphocytes averaged 50 per cent prior to inoculation and at the height of the cough reached 60 per cent. The early loss of weight was again noted. This animal continued well for three months, then succumbed to an ulcerative enteritis. Autopsy revealed no signs of tuberculosis.

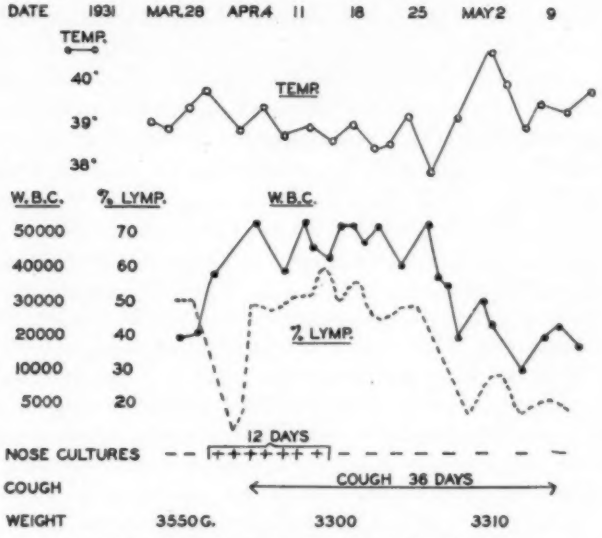

Chart 3.—Experiment 3. Experimental pertussis.

DISCUSSION

The results of the foregoing experiments may be summarized as follows:

After intratracheal inoculation of virulent *H. pertussis* two Erythrocebus monkeys and one *Macacus rhesus* monkey developed a syndrome which closely resembles the disease as seen in man. First, the incubation period varying from seven to ten days observed in these experiments is the generally accepted incubation period of the natural disease. The second comparable feature is the ease of recovery of the organisms early in the illness, the period described in human cases as the "catarrhal phase." It has been definitely established by many observers that it is during this early phase of whooping cough when *H. pertussis* can be readily isolated by the cough-plate method in a relatively high percent-

age of cases. It is of interest to mention here that in this experiment, recovery of the organism was possible only in those animals that developed a pertussis-like illness. Third, the appearance of a cough which gradually became spasmodic and severe, at times associated with vomiting, and which continued for a period of twenty-eight to forty days, is another characteristic symptom of whooping cough. It has been observed in experimental work that spontaneous spasmodic coughs are occasionally noted in monkeys with tuberculosis or other respiratory affections. These factors have been definitely ruled out by the subsequent course of these experimental animals. That the inoculation of the massive doses of organisms per se might presumably be the basis of the cough which developed is highly improbable. In fact it is surprising how much material can be inoculated intratracheally with no cough's developing. The development of a cough was not observed in a large number of attempts even when larger doses of organisms were given, and even following intratracheal inoculations of *H. pertussis* in a group of five monkeys which were suffering from experimental measles infection, conditions most favorable for the production of an irritative cough. (More will be said concerning this fact in another section of this paper.) The rather short duration of the cough and the absence of a whoop in these monkeys are variations which are frequent in clinical experience. Fourth, the gradual rise in white blood cells with a moderate increase in the lymphocytes coincident with the foregoing symptoms is another characteristic feature of pertussis. Variation in the blood picture is seen in normal monkeys but not comparable to the degree observed in these monkeys. Fifth, there was absence of fever which also is characteristic of uncomplicated whooping cough. Sixth, the experimental animal lost weight, which goes hand in hand with the anorexia and vomiting observed in whooping cough, followed by gradual recovery during convalescence. Unfortunately, no conclusive data can be presented as to the nature of the immunity derived. Satisfactory immunity experiments, which were obviously indicated, could not be carried out since the only experimental animal on hand to use as a control was the *Macacus rhesus*. It was later observed that this species of monkey was quite refractory to infection with *H. pertussis*.

In a series of sixteen *Macacus rhesus* monkeys only one developed the pertussis-like syndrome following the intratracheal route of infection, whereas only two Erythrocebus monkeys were used and both developed the syndrome. It is of interest to note that five of the eight successful takes reported by Sauer and Hambrecht[8] were in the Cebus variety of monkeys. Species susceptibility is known to play an important rôle in experimental infections, and it is not unlikely that the monkey, especially the *Macacus rhesus*, is not the ideal susceptible animal to

use in experimental whooping cough work.* In view of the results obtained by Rich, Long, and their collaborators[9] and also by Shibley[10] in apes, this animal presents more favorable possibilities in studies on experimental whooping cough. Unfortunately chimpanzees are too expensive for extended experimentation.

Attempts were also made to implant the *H. pertussis* in monkeys (two Erythrocebus and five *Macacus rhesus*) by the intranasal instillation method. A total of eleven experiments using this method of inoculation proved unsuccessful. The organisms disappeared rapidly following inoculation, and in only one instance was the organism recovered. In this instance the organism was recovered from the nasal passages of an Erythrocebus monkey for a period of twenty days, the animal, however, remaining well.

Table I is a résumé of the preceding experiments.

TABLE I

TYPE OF EXPERIMENT	NO. OF EXPERIMENTS	RESULT		ORGANISMS RECOVERED
		POS.	NEG.	
Intratracheal inoculation	19	3	16	3
Nasal instillation	11	0	11	1

Presumptive evidence has accumulated recently from both clinical observations and animal experimentation which suggests that activation of pathogenic microorganisms may possibily occur at the onset of acute infectious disease by an X factor which is thought by some investigators to be a filtrable virus. The transformation of *H. influenzae* during a common cold from a rough to a smooth form has been demonstrated by Dochez and others.[13] A similar phenomenon has been shown by Shope and Lewis[14] to occur in so-called swine influenza. These workers found that the swine influenza-like organism per se produced negligible results, but the combination of the bacillus with the filtrable form caused a severe illness in hogs. Comparable features exist in the distemper infection of dogs. The frequent association in that disease of *B. bronchisepticus* with a filtrable virus is well known.

Reference has already been made to the probable importance of a virus in whooping cough, and with this notion in mind further studies were planned to apply this concept in an attempt to enhance the susceptibility of monkeys to *H. pertussis*.

II. INTRATRACHEAL INJECTION OF NASAL WASHINGS FROM CASES OF WHOOPING COUGH

The following report deals with attempts to produce experimental pertussis in *Macacus rhesus* monkeys by intratracheal injection of both filtered and unfiltered nasal washings from human cases of whooping

*Two Java and two Capuchin monkeys have been inoculated since with negative results.

cough. The washings were obtained from patients presumably in the first, second, and third weeks of the illness, positive cultures for *H. pertussis* being obtained from the secretions in five instances. A total of thirteen experiments, using unfiltered material, proved unsuccessful. Five other experiments were done using Chamberland filtrates of the above material with negative results. No mild catarrhal affections similar to that described by Rich, Long, Brown, Bliss and Holt[9] in their apes were observed in any of these experiments. Other experiments with filtered and unfiltered washings with superimposed frequent inoculations of recently isolated Bordet-Gengou organisms

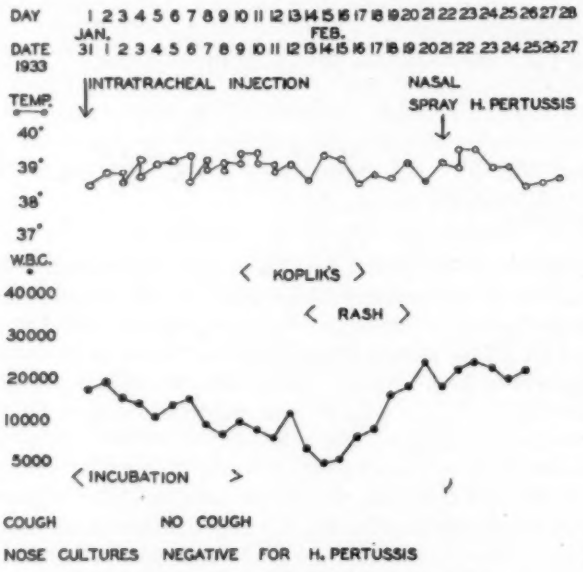

Chart 4.—Experiment 4. Experimental measles.

also proved to be unsuccessful. The negative results obtained in the foregoing experiments with nasopharyngeal secretions from whooping cough patients obviously do not exclude the presence of a specific virus. However, if a virus was present, the monkeys were not susceptible to it.

Table II is a résumé of the results of the preceding experiments.

TABLE II

TYPE OF EXPERIMENT	NO. OF EXPERIMENTS	RESULT	
		POSITIVE	NEGATIVE
Unfiltered nasal washings	13	0	13
Filtered nasal washings	5	0	5

III. INTRATRACHEAL INJECTION OF H. PERTUSSIS IN MONKEYS WITH MEASLES

In view of the negative results obtained with nasopharyngeal secretions, the following experiments were carried out to determine whether successful implantation of *H. pertussis* was more likely in monkeys suffering from an acute infection. Accordingly, it was planned to use the measles virus as an activating agent since monkeys are susceptible to measles and since this disease produces a marked irritation of the respiratory tract.

EXPERIMENT 4. (Chart 4.) Monkey 95, *Macacus rhesus*, male, weighing 3,700 gm., January 31, 1933, was given an intratracheal injection of 3 c.c. saline suspension of virulent *H. pertussis* (three different strains) plus 3 c.c. mixed washings from two cases of measles in the preeruptive and early eruptive stage, respectively. The animal remained well until the tenth day when red macules appeared on the labial mucous membrane; these gradually became numerous. A maculopapular rash which appeared on the face on the thirteenth day later spread to neck, chest, abdomen, and groins. Coincident with the rash, leucopenia was noted. The enanthem faded on the eighteenth day, and the exanthem, on the twenty-first day. The white count gradually rose to normal level on the twentieth day. No cough was noted, and the deep nose cultures remained negative for *H. pertussis*. The animal was inoculated intranasally on the twenty-second day with another strain of *H. pertussis*, but no further symptoms appeared.

Chart 4 is an illustrative record of a series of five monkeys infected with measles, in all of which implantation of *H. pertussis* proved unsuccessful. In three instances measles infection occurred following intratracheal inoculation with washings from human cases of measles and in two instances following exposure to one of the monkeys in the preeruptive period.

Virulent *H. pertussis* organisms were inoculated simultaneously with the measles washings, and subsequently during the course of the measles illness another strain of virulent *H. pertussis* was instilled in the nasal passages of the three experimental animals. No cough nor symptoms suggestive of whooping cough appeared. The rapidity with which *H. pertussis* disappeared from the upper respiratory passage was striking. Usually within twenty-four to forty-eight hours after inoculation the deep nose cultures became negative. Although massive doses of organisms (3 c.c. of a saline suspension) were inoculated, no "irritative" cough was noted. Rich[15] has raised the question in his article, "The Pathogenesis of Whooping Cough," whether "any one of a number of pathogenic bacteria might provoke tracheitis, bronchitis, and coughing if introduced intratracheally in such quantities." Yet, in these experimental animals under conditions which would presumably favor the occurrence of an irritative cough, no cough was noted.

SUMMARY

1. A pertussis-like syndrome was noted in one *Macacus rhesus* and two Erythrocebus monkeys following intratracheal inoculations of viru-

lent *H. pertussis* organisms. The criteria for infection presented were: (1) incubation period of seven to ten days; (2) recovery of organism early in the illness; (3) leucocytosis with a predominance of lymphocytes; (4) cough which became spasmodic, lasting twenty-eight to forty days with subsequent recovery.

2. Inoculation in *Macacus rhesus* monkeys with filtered and unfiltered nasal washings from cases of whooping cough gave negative results. Combinations of filtered washings and organisms also proved negative.

3. Measles virus did not favor implantation of *H. pertussis* in *Macacus rhesus* monkeys.

CONCLUSIONS

1. Experimental results which add further support to the bacillus of Bordet and Gengou as the specific agent in whooping cough are presented.

2. The monkey is probably not the ideal animal for experimental whooping cough investigation.

The authors express their grateful appreciation to Dr. James D. Trask for his assistance in this study.

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ENTERITIS IN INFANTS: PREVENTION OF ITS SPREAD

Dick Diet Kitchen and Aseptic Nursery Technic

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TO NURSE at the breast was, through the ages, the only protection against infantile enteritis. At the close of the nineteenth century Budin,[1] the Paris obstetrician, made the clinical observation: "In sterile milk alone is safety, and it must be made the basis of all artificial feeding." Chapin[2] in 1915 found a high infant death rate persisting in institutions. In the state of New York, in eleven asylums for infants, it ranged between 18.3 and 57.6 per cent with an average of 42.3 per cent. In ten institutions in various American cities it varied between 31.7 and 75 per cent! For infants of the same class in boarding homes he reported a mortality of but 12 per cent. Through concerted efforts, such as the infant welfare movement, the purification of drinking water, the pasteurization and boiling of milk, and prophylactic pediatrics, the "summer peak" of infant deaths gradually disappeared. Were it not for reliable epidemiologic data, it might seem that modern infant feeding had completely triumphed over infantile enteritis. The League of Nations' report on enteritis[3] shows that it persists as a leading cause of infant deaths in all countries and large cities. In the United States birth registration area (26 states), enteritis caused 17,291 infant deaths in 1930, 14,021 in 1931, and 10,791 in 1932.

This disease, highly contagious for young bottle-fed infants, wreaks havoc wherever it gains access. Its communicability is seldom sufficiently stressed. Newborn infants, who spend less than the first fortnight in modern maternity nurseries, are relatively safe. That this security rests more on the absence of the causative microorganism than on the nursery technic is evinced by the periodic outbreaks of this bane of the neonatal nursery. Infants at home on the breast, or on supervised, boiled feedings are, likewise, more protected by their isolation than by the household technic. The out-patient infants with enteritis prove that their protection is only relative. Although the carnage of a former day no longer exists, institutions housing artificially fed infants from diverse sources still show a comparatively high incidence of enteritis. This prevalence is, in no small measure, due to secondary cases. Not the absence of enteritis, but its presence without a secondary case over long periods of time, is the ultimate test of a precautionary technic. To prevent the spread of enteritis and other infections, many hospitals, infant asylums, orphanages, day

nurseries, and boarding homes have instituted sterilized food, cubicles, and special nursery rules.

When The Cradle opened in 1923 for the care of homeless infants until their adoption,* the diet kitchen and nursery technic of a leading infant hospital were expected to meet any emergency. The infant, on admission, was placed in an isolated, cubicled crib with "special precautions" technic for a fortnight and admitted to the general nursery if well at the end of that time. Morbidity and mortality remained low for years. With twenty deaths in four years, the mortality rate was 4.8 per cent. Eighteen of these deaths were due to enteritis; eleven of the infants had contracted it in the institution. Scattered over a period of four years, these deaths were charged to "the hazards of institutional care of homeless infants." Because enteritis would often be absent for months at a time, there seemed to be no reason to question the efficacy of the precautionary technic.

Two infants (No. 462 and No. 463), born in Chicago hospitals, were admitted on Feb. 3, 1927. Both developed enteritis; one child died within a few days; the other developed complications, including mastoiditis. Because they typify the two forms of enteritis encountered in the epidemic which followed, excerpts from the clinical, nursing, and postmortem notes follow.

CASE 1.—(No. 462) Clifton was born Jan. 17, 1927; weight, 6 pounds 6 ounces. He was admitted, Feb. 3, 1927, when he weighed 6 pounds 10 ounces. Entrance examination was negative. Blood, stool, urine, nose and throat cultures, rectal temperature, etc., were normal.

February 4 to 8: He was apparently well; stools apparently normal. February 9: His weight was 6 pounds 14 ounces; rectal temperature, 100.4° F.; he was fretful, had moderate abdominal distention, refused food, and vomited; he passed four semiliquid stools with curds and mucus, last two containing blood. February 10: Rectal temperature was 103.4° F.; abdominal distention increased; pallor increased; he was toxic, had irregular respirations, and died.

Anatomic Diagnosis (Dr. J. Lisle Williams): Acute hemorrhagic enteritis; acute hyperplasia of mesenteric lymph nodes; acute fibrinopurulent peritonitis.

CASE 2.—(No. 463) Sybil, was born Feb. 1, 1927, and weighed 6 pounds 10 ounces. She was admitted Feb. 3, 1927, weighing 5 pounds 14 ounces. Entrance examination was negative. Nose and throat cultures, vaginal smears, blood, urine, stool, and rectal temperature were normal.

*Infants unfit for adoption are not admitted, or promptly returned to the mother, or transferred to a suitable institution. Congenital syphilis is rarely encountered, because reputable laboratories perform Wassermann tests on the mothers' blood, usually before the infants are admitted. Excluded are infants with: syphilis, gonorrhea, tuberculosis, gross anomalies, gross congenital defects, birth paralysis, brain injuries, mongolism, cretinism, etc. Insanity, hereditary nervous diseases, chronic alcoholism, etc., in either parent, debars the infant. Early legal adoption of the healthy, illegitimate infant, by carefully selected foster parents, eager and able to care for the infant as their own, appears to be a rational solution to this age-old problem. A theory, occasionally promulgated by psychologist or social welfare worker, that the state legally compel all unwed mothers to keep their offspring for at least a year, would force many more girls to risk the hazards of criminal abortion; many more infants would die from enteritis or other infections; of those who might grow up, not a few would become a burden to the state. With a declining birth rate, the urgency of saving these infants increases in importance. The Cradle's method is a step forward in social evolution, because it is now the safest and most humane plan devised for the unwed mother and her child.

February 4 to 15 she was apparently well; there was a slight gain in weight, and the stools were apparently normal. February 16: Weight was 6 pounds 10 ounces; rectal temperature, 100.4° F.; she was fretful, had moderate abdominal distention, refused food, vomited and was pale. She passed four semiliquid, brown stools of foul, musty odor. February 17, 18: She was rather listless; stools as above. February 19: Weight was 5 pounds 10 ounces; rectal temperature, from 102.8° F. to 104° F.; pulse, 170; respirations, 44; bilateral myringotomy performed by attending otologist.

February 21: Weight was 5 pounds 4 ounces; rectal temperature, 103° F.; abdominal distention increased. She was transferred to the hospital; bilateral mastoidectomy was performed and the infant died.

Anatomic Diagnosis (Dr. J. Lisle Williams): Bilateral, acute, suppurative otitis media and mastoiditis; acute, generalized fibrinopurulent leptomeningitis and ethmoiditis; septic thrombosis of lateral venous sinuses; hyperemia of intestinal wall; hyperplasia of mesenteric lymph glands; submucous hemorrhages of stomach and colon. Smears and cultures from ear and mastoid wound; streptococci in chains. Spinal fluid culture: *B. coli*.

During the following eight months, eighty-six infants contracted enteritis. The twenty-seven deaths of 1927 were due to enteritis; twenty-one of these infants developed the first symptoms after they had been in the institution longer than ten days (Table I). When the customary attempts at eradication of the infection (complete change of nurses, disinfection and painting of the entire nursery, etc.) were of no avail, Dr. Gladys H. Dick, a director and benefactor of The Cradle, in collaboration with Dr. George F. Dick and Dr. J. Lisle Williams[4] undertook a complete bacteriologic investigation. When the lactose-litmus-agar plate method of culture was used, they recovered the Morgan dysentery bacillus from the intestinal lesions of all infants who died. "The Morgan dysentery bacillus isolated was highly pathogenic for rabbits. From 1 to 3 c.c. of the whole, forty-eight-hour broth culture, injected intravenously, killed rabbits in from eight to forty-eight hours. From 3 to 5 c.c. of sterile filtrate from forty-eight-hour broth cultures. injected intravenously, killed rabbits within twenty-four hours. The rabbits which received the sterile filtrate and those which received the whole broth cultures showed hemorrhagic enteritis."

Because the infection was apparently of intestinal origin, all feedings and water were boiled ten minutes; bottles and nipples were autoclaved. As some of the infants who contracted enteritis were on powdered protein milk dilutions (which were not boiled to prevent curdling), a bacteriologic examination of the various ingredients of all feedings was undertaken by Dr. George F. Dick and Dr. Gladys H. Dick.[5] Unopened cans of these powdered milk preparations, when cultured, were found to contain a variety of living bacteria, including streptococci.* The epidemic came to an abrupt end in November—soon after only sterilized food was given to all infants.

*The A.M.A. Committee on Foods has since been instituted to approve and regulate the purity of foods.

TABLE I

THE CRADLE ADMISSIONS AND DEATHS FOR TWELVE YEARS

	(AN APPROVED TECHNIC DURING FIRST SIX YEARS)							(DICK TECHNIC DURING LAST SIX YEARS)						
	1923	1924	1925	1926	1927	1928	6 YR. TOTAL	1929	1930	1931	1932	1933	1934	6 YR. TOTAL
Admissions	65	83	130	157	257	250	942	254	320	271	253	272	250	1,620
Deaths	2	6	5	7	27	8	55	5	1	3	4	3	1	17
Enteritis deaths	2	6	5	5	27	8	53	5	0	0	0	1	0	6
Fatal enteritis (contracted at The Cradle)	2	4	4	1	21	8	40	0	0	0	0	0	0	0
	5.8% mortality rate, first 6 yr. 96.0% of deaths due to enteritis 75.0% of fatal enteritis contracted after admission							1.0% mortality rate, last 6 yr. 35.0% of deaths due to enteritis. None contracted after admission.						

That the spread of enteritis may be due to flaws in nursery technic is verified by what happened soon after the subsidence of the 1927 epidemic. Malcolm (No. 680), admitted on Dec. 16, 1927, came from an obstetric nursery in Chicago where enteritis was endemic. He was placed in a cubicled crib under the customary "special precautions" technic. The course of his illness was quite like that of Sybil (see above). He died Jan. 29, 1928. On February 15, Philip (No. 699), a thriving infant, admitted five weeks previously, developed enteritis and died ten days later. In May, three infants (Nos. 769, 792, and 795), developed fatal cases of enteritis weeks after admission.

As only sterilized food had been given to all infants, Dr. Gladys Dick made a detailed survey of the nursery and feeding technic. Cotton applicators for cleansing nostrils, made by the nurses (some of them on relief duty with enteritis cases), were being used promiscuously without sterilization. Nurses who bathed the babies and changed diapers also gave feedings. This and other evidence led to the conclusion that *the causative organisms, from the feces of an infected infant, on the nurses' hands, resist washing and contaminate the nipples, supplies, and food of other infants.* "To avoid transmission of the infection by the fingers, nurses were required to put on a fresh pair of sterile rubber gloves for each feeding of each baby and for giving water. Since precautions were also taken in the diet kitchen and throughout the institution, no finger was allowed to come in contact with anything that went into a baby's mouth. Diapers of all infants were put in lysol solution immediately on removal." Since 1928 everything that entered an infant's mouth or nose was sterilized and was not touched except by aseptically clean hands. In 1929 five of the infants, who had enteritis when admitted from Chicago hospitals, died, but no new case of enteritis occurred at The Cradle. Each year since then, infants have been admitted with enteritis, gonorrhea, and acute upper respiratory disease, but no secondary case has occurred. In 1933 one of the infants admitted with enteritis recovered after an illness of four months; another died ten days after admission, but no new case developed.

The absence of a secondary case in six years, during which time 1,620 infants were cared for, is unique for institutions of this kind, and proves the Dick technic flawless. Without sacrificing safety, various minor changes have been made for the saving of time, labor, and material. Because Dr. Dick's various suggestions involve diet kitchen, cubicle, nursing and medical care and have been incorporated as integral parts of The Cradle technic,* a synopsis is appended:

A unit consists of twelve cubicled cribs, housed in several small communicating rooms. Each unit has its own nurses and supplies. A graduate nurse and two student nurses do twelve-hour day duty; a

*For practical suggestions, thanks are due Miss Dorothy Lopnow, R. N., supervisor.

graduate and student nurse do twelve-hour night duty. Only these nurses, resident, and attending physicians have access to a unit.

The graduate nurse on day duty is responsible for her unit. She has sole charge of infants weighing less than 6 pounds (in incubators), sick infants, medication and treatments; she takes all cultures and smears, accompanies the attending pediatrician, consultant, and visiting physician; she supervises the work of student nurses, prepares for the diet-kitchen nurse a list of each infant's twenty-four-hour feedings, records on each infant's chart (from the student nurses' notes) weight, rectal temperature, number and quality of stools, urinations; she records food intake, refused and vomited. To the resident she reports fever, distention, repeated vomiting, diarrhea, discharges, skin lesions.

The student nurse gives feedings, weighs, bathes, and clothes the infants, and changes diapers. Her daily observation sheet for each infant is transcribed into the infant's records by the supervising nurse.

The attending pediatrician puts on a clean gown and mask* before he enters a unit. He scrubs his hands with running water, soap and brush, and soaks them in the "clean" basin of disinfectant solution,† then dries on a clean towel. The undressed infant is examined in the crib; the "clean" supervising nurse hands him a "clean" stethoscope, sterile tongue blade, and ear or nose speculum from a "clean" tray. His hands and the stethoscope bowl are then soaked in the disinfectant solution and dried on a clean towel before he proceeds to the next infant. At the conclusion of a visit the resident's findings and the nurses' records of new infants, sick infants, and those ready for adoption are read; he countersigns the resident's notes, if correct, and signs the chart when the infant is discharged. Two regular visits are made each week. Besides the preliminary examination, a final examination is made of each infant at the end of four weeks—the minimum stay—before an infant is recommended for adoption. Consulting dermatologist, surgeon, otologist, psychologist, etc., observe the above precautions.

The resident physician follows the precautionary technic outlined above. He records the complete physical examination of each infant soon after admission and underscores with red ink findings which deviate from the norm. He examines nose and throat cultures, vaginal and eye smears, urine, blood, and stools in the well-isolated laboratory. He takes blood (for Wassermann test) from the heel of infants over three months of age. He prescribes medication and treatment, when indicated, between the attending physician's visits.

*Masks (two layers of handkerchief linen) are worn by everyone in the nursery proper; a removed mask is replaced by a clean one. Used masks are boiled for ten minutes, then washed with soap and water, rinsed and dried.

†One tablespoonful of lysol or klomine to a quart of water.

Visiting physicians, who examine infants for prospective foster parents, do not enter the nursery proper. They put on clean gowns, and masks, and wash their hands in running water. The naked infant, wrapped in a clean sheet, is placed on the examining table in the "showroom," which adjoins each unit. The physicians use only the clean stethoscope and sterile supplies from the "clean" tray.

Adopting parents never enter the nursery. The infant, in clean linen, is placed in a crib in the showroom, where the adopting parents, in gowns and masks, are permitted to hold, not to fondle or kiss the infant. When the infant is returned to the cubicle crib, the clothing is changed. Visitors never enter the nursery. Those over sixteen years of age are permitted to look at the infants through the glass doors leading to the nursery.

Each room has a linoleum floor (mopped daily with hot suds), good natural and artificial light, electric ventilator, hot water heat, humidifier, kitchen sink, hot and cold water (foot-pedal faucets), drain board, large saucepan (for warming bottles), a large bowl of disinfectant solution (for used bottles and nipples), a basin of disinfectant solution marked "clean," another marked "contaminated," scales, and sterile forceps in an open jar of disinfectant solution. All floors are "contaminated"; anything dropped is disinfected or put into the wire hamper. Linen soiled with urine or feces is thrown into the hopper can. The corridor walls, windows, and shelf where the feedings are warmed are "clean." Walls are wiped, twice weekly, with disinfectant solution (as far as can be reached). Sinks are "contaminated."

A cubicle contains a standard (white) crib (42×22 inches), low chair, a shelved, enameled bedside table with attached bath-basin (for bed bath), a day's supply of clean linen (sheets, diapers, undershirts, gowns, towels), soap. On the top of the bedside table are arranged sterile glass jars with cotton balls (for cleansing buttocks), sterile jars of applicators and gauze squares, 8 oz. bottle of saturated solution of boric acid (for routine cleansing of buttocks), sterile mineral oil, sterile vaseline, and rectal thermometer in vial of disinfectant solution. A properly folded gown (for student nurse) hangs on a hook in the cubicle. An open paper bag is pinned to the table for waste cotton, etc. To permit ventilation, the glass partitions are only five feet high.

Within a cubicle an individual, aseptic technic is used. Everything is "clean" for that infant but "contaminated" for the other infants. Twice a week the cubicle walls and everything in the cubicle is wiped with a cloth saturated with disinfectant solution. The infant remains in the assigned cubicle, until ready for adoption; transfers are never permitted. After the infant's discharge, the bed and table are stripped; cubicle walls, crib, table, and chair are wiped with cloth saturated with disinfectant solution; crib and mattress are aired out-of-doors for twenty-four hours; the mattress is whisked with disinfectant solution.

The next day the bed is made up with clean linen, the bedside table equipped with sterile supplies and clean linen.

At the feeding hour a bottle from each infant's bottle rack in the refrigerator is brought to the nursery in a bottle rack, which is placed in the deep saucepan of hot water. After the supervising nurse of the unit scrubs, disinfects, and dries her hands, she puts on sterile rubber gloves, removes bottle caps, puts on sterile nipples, and covers each nipple with a sterile, creased (four-ply) gauze square (4×4 inches). The student nurse scrubs, puts on a cubicle gown; the diaper* is changed if soiled; her hands are then scrubbed with soap, sterile brush, and running water, then soaked in the "contaminated" basin of disinfectant solution, then in the "clean" basin of disinfectant solution; she dries them on clean towel. She then sits on the cubicle chair with the infant in her left arm, carefully removes the gauze without touching the nipple, and inserts the nipple into the infant's mouth without touching the upper part of the bottle. If nipple needs changing, the "clean" supervising nurse makes the change; if bottle gets cold, the student nurse warms it under the hot tap. Food not consumed is poured into the sink drain; the empty bottle and nipple are promptly submerged in the large pan of disinfectant solution. The student nurse then scrubs, unties gown, scrubs, takes off gown, hangs it on hook on cubicle wall, with the "contaminated" side out, scrubs hands and arms up to elbows, soaks in "clean" basin of disinfectant, dries on clean towel, and goes to next cubicle where each step of the procedure is repeated. After all infants have been fed, the bottles and nipples are scoured with hot suds, and rinsed; the inverted bottles in the rack are placed in the diet kitchen autoclave until they are sterilized the next morning.

Before the daily weighings the scales are wiped with a cloth wet with disinfectant solution. They are then balanced with a clean diaper. The student nurse puts on a cubicle gown, and places the stripped infant in the scoup. A square of clean paper is used to handle the weights; the weighed infant and diaper are placed in the crib; the infant is then bathed and dressed. After the washing of the hands (see feeding technic) the gown is placed on the cubicle hook, and the hands are again washed; a clean diaper is spread in the scoup. The student nurse then goes to the next cubicle and repeats each step of the procedure. Should the scales become contaminated, they are cleansed with disinfectant solution before they are used again.

The diet kitchen contains a gas-fired autoclave, gas range, kitchen sink with hot and cold water (foot-pedal faucets), kettles, deep sauce-

*Soiled diapers and linen soiled with feces are soaked in the pail of disinfectant in each room. Recently, an aseptic diaper service delivers sterile diapers in tin containers each day and calls for all soiled diapers.

pans, sieve funnels, and tagged wire bottle racks. A graduate nurse supervises the work of the student nurse who prepares the feedings. While the pyrex bottles, rubber bottle caps, nipples, and utensils for measuring and mixing the food are autoclaved at 15 pounds for fifteen minutes, the graduate nurse computes the amounts of the various ingredients required for the preparation of the twenty-four-hour supply of food for all infants. Most of the feedings are simple stock formulas; a card for each infant is in view on the wall. The student nurse measures, weighs and mixes the ingredients, and then puts on a long-sleeved sterile gown, mask, cap, and sterile rubber gloves. A sterile sheet is spread on the table; the hot bottles are removed from the autoclave, lined up, and covered with the sheet until they are filled. The strained food is boiled in deep saucepans for ten minutes, measured into the sterile nursing bottles, capped, and promptly refrigerated. The infant's name is written on each bottle with a blue glass-pencil while bottles are warm. Or, the bottles, containing the measured feedings, are covered with perforated rubber bottle caps, autoclaved at 15 pounds for five minutes, and then refrigerated.

The wet-nurse station, adjoining the diet kitchen, is in charge of the diet kitchen nurse. An electric breast pump is used twice daily on lactating mothers of the vicinity who sell their milk. The strained, pooled milk in sterile pyrex bottles is placed in a deep saucepan containing water up to the milk level; after the water has boiled for twenty minutes, the bottles are cooled and refrigerated.

DISCUSSION

Because two graduate and three student nurses for the twenty-four-hour care of twelve infants seemed excessive to several of the medical authorities acquainted with the Dick technic, the average cost per infant for the first and second six-year periods has been computed. During the last six-year period (with Dick technic) the cost per infant averaged 26 per cent less than it did with the standard technic. During the first six years the average number of occupied cribs was twenty-eight; during the last, it was twenty-three. Because of the relative absence of illness, most of the full-term infants are now ready for adoption at the end of a month—the arbitrary minimum stay. Six hundred seventy-eight more infants were cared for during the last six years than in the first six years. The admission of infants with enteritis from boarding homes and nurseries (where enteritis was present), without the occurrence of a secondary case at The Cradle in the last six years, is proof that the Dick technic is flawless. To sterilize the food and not use an aseptic nursery technic is like an operating room in which only the instruments are sterilized.

SUMMARY

Vital statistics show that enteritis is still a prevalent cause of death in young infants. It spreads by way of contaminated food, nipples, and supplies. Anything intended for an institutional infant's nose or mouth should never be touched after it has been sterilized. The aseptic, individual nursery technic perfected by Dr. Gladys Dick in 1928 has made it possible to care for 1,620 homeless infants, without the occurrence of any cross-infection. It is sound economy because it reduces morbidity and prevents unnecessary deaths.

CONCLUSION

A six-year trial of the Dick diet kitchen and individual, aseptic nursery technic at The Cradle, without cross-infection enteritis, proves the technic flawless. The cost is not excessive. It is sound economy. The per capita cost per day is less than with the precautionary technic formerly used; without secondary cases of enteritis, the perennial morbidity is reduced, and there are no unnecessary deaths.

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MENINGOCOCCUS INFECTIONS

An Analysis of 120 Cases in Children

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THE purpose of this paper is to present in a statistical way the information obtained from a study of a series of 120 cases of meningococcus infections observed in the St. Louis Children's Hospital during the ten-year period, 1924 to 1934, in order that comparisons may be made with the observations in other localities.

Contact Infections.—Although it is somewhat rare to observe more than a single case of meningococcus meningitis in a family, five of our patients were definitely exposed to the disease by contact with another member of the family who had meningitis. In another case a brother had had meningitis eight months earlier.

Association With Other Disease.—The possible relationship of the onset of meningococcus infection to upper respiratory disease is of some interest. Ten patients had had upper respiratory infection for at least one week before the onset of meningeal signs. Two patients had congenital heart disease, and two had rheumatic heart disease. One patient had had a skull fracture nine months before the attack of meningitis. The history of intracranial birth injury was obtained twice. The diagnosis of bronchopneumonia was made in three patients before they developed signs of meningococcus infection.

Duration of Disease.—The average duration of illness before admission to the hospital was 5.4 days. However, if the eleven cases which had become chronic are omitted, the average duration would be only 3.5 days. The average stay in the hospital for the 120 patients was eighteen days. The average for the seventy-six patients who recovered was twenty-four days. It is of some interest to note that one patient remained in the hospital for six months because he was considered a carrier. He recovered from the attack of meningitis in about two weeks, but meningococci were cultured repeatedly from the throat even after the tonsils and adenoids were removed. Finally the organisms were found to be nonvirulent, and the patient was discharged. This was the only carrier diagnosed in our series. The average stay in the hospital for the forty-four patients who died was 7.3 days. If the three patients who had relapses are omitted, the average would be five days. Patients in eighteen of the fatal cases died within twenty-four hours after admis-

From the St. Louis Children's Hospital.
Read before the St. Louis Pediatric Society, St. Louis, Mo., October 19, 1934.

sion and obviously could have received very little treatment. Only thirteen patients of these forty-four fatal cases were in the hospital for more than two weeks.

Relative Frequency of Clinical Signs.—The symptoms and signs observed with the percentage of frequency are given in Table I. In the last four the records were not complete.

TABLE I

SYMPTOM	PERCENTAGE PRESENT	CASES OBSERVED
Fever	99.2	120
Drowsiness	86.7	120
Neck rigidity	83.3	120
Vomiting	75.8	120
Headache (older children)	61.7	68
Unconsciousness	40.0	120
Convulsions	30.0	120
Chills	11.6	120
Strabismus	15.8	120
Abdominal pain	6.7	120
Positive Brudzinski reflex	68.4	79
Positive Kernig reflex	61.3	106
Absent abdominal reflexes	50.0	24
Deep reflexes		101
Normal	39.6	
Hyperactive	23.8	
Sluggish	20.8	
Absent	15.8	

The laboratory findings are given in the following tables.

TABLE II

SPINAL FLUID		WHITE BLOOD CELLS	
CELL COUNT	CASES	CELL COUNT	CASES
Under 1,000	20	Under 10,000	14
1- 3,000	25	10-15,000	22
3- 6,000	12	15-20,000	23
6- 9,000	12	20-25,000	27
9-15,000	8	25-35,000	14
		Above 35,000	11

TABLE III

	AVERAGE	CASES OBSERVED
Polymorphonuclear cells in blood	76%	100
Polymorphonuclear cells in spinal fluid	88%	49

Urine:		
Albumin—(trace to ++, mostly trace)	in 36 of the 93 cases	(38.7%)
Sugar—	in 2 of the 89 cases	(2.2%)
Microscopic		
White blood cells or casts—	in 8 of the 91 cases	(8.8%)
Meningococci found:		
Smear from spinal fluid	92 of 111 cases	(82.9%)
Culture from spinal fluid	75 of 92 cases	(81.5%)
Culture from blood	23 of 50 cases	(46.0%)

Serum Treatment.—Antimeningococcus serum was given routinely by the intraspinal route. In addition, many patients from the first received serum either intracisternally or intraventricularly, alternating with intraspinal therapy. If any difficulty was encountered, particularly in cases of block, the serum was given repeatedly into the cistern or the lateral ventricles. Serum was given intravenously and intramuscularly in those cases in which it was thought septicemia was present because of skin petechiae or when the patient was seen soon after the onset of symptoms. It is a generally accepted fact that meningococcus meningitis is always preceded by a blood stream infection although this infection usually persists for only a short period of time. When serum was given intravenously, it was diluted with five to ten volumes of Ringer's solution and was given by gravity.

TABLE IV

ANTIMENINGOCOCCUS SERUM GIVEN

ROUTE	CASES	NUMBER OF INJECTIONS	AVERAGE AMOUNT	
			EACH INJECTION	EACH PATIENT
Intramuscular	12	24	14 c.c.	28 c.c.
Intravenous	55	82	21 c.c.	32 c.c.
Intrathecal	108	688	18 c.c.	114 c.c.

Serum sickness was observed in 64 of the 97 possible cases, an incidence of 64.9 per cent. The average time of appearance was the seventh day after the first injection of serum. When present, it occurred between the fourth and twelfth days. The incidence of serum sickness in children under three years of age was about 12 per cent higher than in children over three years of age, corrected for morbidity incidence. The usual manifestation was urticaria with an occasional slight elevation of temperature. Arthritis was noted in three patients.

Some immediate reaction followed the administration of serum to eleven patients. Five of these received serum intravenously and six, intraspinally. Four types of reaction were observed after intravenous serum. Two patients became restless, coughed, and collapsed but soon recovered. They had serum sickness on the sixth day. One patient had a chill and a rapid pulse. Accelerated serum sickness was observed once, urticaria appearing in ten minutes after the serum and then again on the third day. One patient died a few minutes after serum was given into the longitudinal sinus. He had a convulsion and became cyanotic with shallow respirations. The cause of death could not be determined definitely as an autopsy was not permitted. Five patients reacted similarly after the injection of serum intraspinally. They collapsed and had irregular respirations and tachycardia but promptly improved. One of these patients had had no reaction after intravenous serum on the preceding day. One patient, who was moribund when admitted to

the hospital and had been ill for four days, died forty minutes after receiving serum intraspinally.

Morbidity and Mortality.—In this series of cases the morbidity incidence in females and males was identical. This observation leads to the conclusion that in children the disease is not more common in males than in females. In adults, the higher incidence in males probably may be explained on the basis of greater exposure and by the fact that many statistical reports deal with meningitis in army camps.

The incidence of the disease and the mortality, in relation to age are presented in Chart 1. The highest incidence was found during the first six months of life. In general this corresponds with the reports of other investigators. However, the diagnosis in infants is frequently more difficult to make than in older children, and for this reason many infants may have come to us without a diagnosis of meningitis, while some older

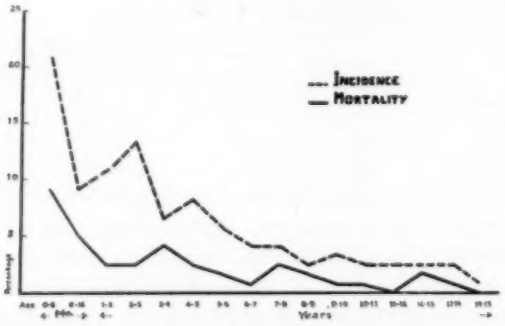

Chart 1.—The relation of age to incidence and mortality in 120 cases of meningococcus meningitis.

children with a presumptive diagnosis were probably sent directly to the Isolation Hospital. Forty-four of the 120 cases terminated fatally, as a result of the infection, a mortality rate of 36.6 per cent. One patient was discharged unimproved in three weeks with a marked internal hydrocephalus, and one patient with obstructive hydrocephalus returned one month later and died. With these two cases included, the mortality rate would be 38.3 per cent. It is frequently stated that in children the highest mortality is during the first two years of life. The mortality rate in this series was 40.8 per cent for children under two years and 33.8 per cent for children over two years.

The number of cases reported in the city of St. Louis each year during the ten-year period is compared with the number of cases in the St. Louis Children's Hospital. The two curves correspond very closely and for each year are in a proportion of 8:1 (Chart 2). An epidemic occurred in 1929.

The incidence of the disease was most common during the winter and spring months, the highest incidence being in February and March (Chart 3).

The most important complications that developed were hydrocephalus, deafness, ocular disease, and otitis media. Bronchopneumonia was very infrequent even in the fatal cases in contrast to the usual reports. The diagnosis of hydrocephalus was made in nine cases, death resulting in

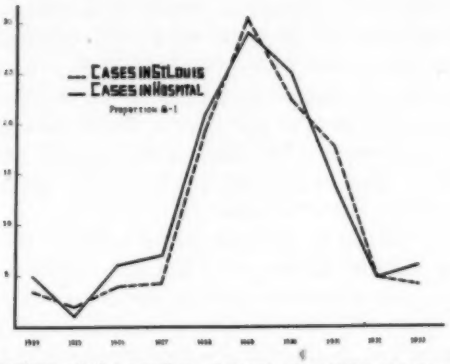

Chart 2.—Comparison of the number of cases of meningococcus meningitis in the city of St. Louis with the number of cases in the St. Louis Children's Hospital, 1924 to 1934.

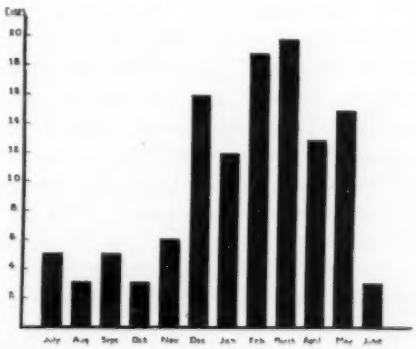

Chart 3.—Monthly incidence of 120 cases of meningococcus meningitis, 1924 to 1934.

four. Definite obstruction was demonstrated in four patients and communication, in three. The type of hydrocephalus was not determined in the other two patients.

Eight cases of deafness were observed. Thus 10.5 per cent of the patients who recovered were deaf. This result is slightly high, and no explanation can be given for it. The deafness was always permanent. The eye complications that were noted were iridocyclitis, iridochoroiditis, uveitis, iritis, and papilledema. The eyes were involved in twelve patients,

an incidence of 10 per cent. Otitis media was present in 17.5 per cent of the patients.

Three of the 120 patients had relapses and died; they were 5 months, 6 years, and 5 years of age. The duration of the disease was nineteen, thirty-five, and seventy-four days, respectively. Antimeningococcus serum was given on repeated occasions.

Meningococcus septicemia without involvement of the meninges was observed in three patients. Two of them recovered promptly after serum was given intravenously. The third patient died sixteen hours after the onset of symptoms; 45 c.c. of serum were given intravenously, but this therapy was not beneficial. The spinal fluid in four patients was found to be clear without an increase in the cell count, but meningococci were cultured from the spinal fluid and blood. These cases were recorded as meningococcus septicemia with involvement of the meninges without cellular response. They were treated, but all four died within twenty-four to forty-eight hours after onset of the illness.

Petechiae were found in sixty-six patients, or 55 per cent, although in five of these records the nature of the skin lesions was questionable. Petechiae were present in twenty-two of the twenty-three cases in which meningococci were cultured from the blood, or conversely only one positive blood culture was obtained where petechiae were not present. Blood cultures taken from thirty-seven patients in whom petechiae were present were reported positive for meningococci in 59.4 per cent.

Nine patients in this series were admitted to the hospital with a history suggestive of meningeal irritation for a period of three to four weeks. The diagnosis of chronic meningitis will be used arbitrarily in the discussion of these cases. They were not in any way comparable to the chronic basilar type of meningitis. Most of these children presented a history of fever, vomiting, irritability, and rigidity of the back and neck, present for several weeks. Seven of these patients responded very promptly to antimeningococcus serum therapy and apparently were well when discharged from the hospital. Death occurred in two before more than three injections of serum could be given. One patient returned one month after discharge and died. Autopsy revealed a marked internal hydrocephalus but no evidence of meningitis. All cultures were negative for meningococci at that time. It is suggested from this study that a subacute or chronic infection of the meninges with the meningococcus is not uncommon and that the duration of the disease cannot be used as a clinical point in ruling out epidemic meningitis.

Autopsies were performed in 47.7 per cent of the fatal cases.

CONCLUSIONS

One hundred twenty cases of meningococcus infections occurring in the St. Louis Children's Hospital during the ten-year period, 1924 to 1934, are reviewed from a statistical standpoint with the following observations:

1. The highest incidence was found during the first six months of life.
2. There was no difference in sex incidence.
3. The disease was most common during the winter and spring months.
4. Meningococcus septicemia without meningeal involvement was present in three patients, two of whom recovered.
5. Chronic meningitis was present in nine patients.
6. Serum sickness occurred in 64.9 per cent of the patients.
7. Relapses occurred in only three patients, all of whom died.
8. The mortality rate was 38.3 per cent.

STREPTOCOCCUS MENINGITIS IN SCARLET FEVER

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THE diagnosis of suppurative meningitis in scarlet fever advanced from a status of opinion and sometimes conjecture to an approximation of fact when Hirsch[1] in 1900 first used lumbar puncture in differentiating the various cerebral manifestations that occur with this disease.

Reported cases of scarlatinal meningitis undoubtedly fail to represent the actual frequency. With uncommon conditions of high fatality, the tendency is to report recovered cases and to neglect the others. Because streptococcus meningitis in scarlet fever is so uncommon, no ordinary group of patients with scarlet fever can give a satisfactory index of the actual frequency of the condition. The frequency and nature of streptococcus meningitis among 17,311 recent patients with scarlet fever is presented in this report, with the purpose of giving an approximate idea of present-day conditions. Collected reports of a number of observers, although having the value of significant numbers, do not have the reliability of a similar group from a single clinic.

All available records of scarlatinal meningitis were reviewed by Benard[2] in 1909. Fourteen cases were eliminated from his analysis because of inexact diagnosis. Twenty-eight others were substantiated as meningitis. The clinical descriptions were adequate, and all had been confirmed by examination of the cerebrospinal fluid or by necropsy. This was considered the probable number of authentic reported instances of purulent meningitis in scarlet fever up to that time.

Nineteen additional cases have been reported since then, eleven[3-5] without detailed description, eight by case reports.[6-12] Five of the nineteen patients recovered, those of Delger, Neal and Jones, Neal, Ohnacker, and one of Zischensky's. This is not representative of the usual fatality rate. Many fatal cases doubtless were not reported; perhaps several hundred in the course of the twenty-five years since Benard's review. His collected report of the observations of a number of investigators previous to 1909 showed the incidence of purulent streptococcus meningitis in scarlet fever to be nine cases among 13,550. Our series represents consecutive observations by the same persons from 1926 to 1933. The indicated frequency of the condition is somewhat greater, in that nineteen cases occurred among 17,311 patients with scarlet fever. Both

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series include only hospital patients. The frequency for scarlet fever in general would likely be less. Purulent leptomeningitis is certainly one of the rarer complications of scarlet fever, but it is important because of its high fatality.

ETIOLOGIC FACTORS

The age distribution of scarlet fever meningitis was not that of scarlet fever. Only two cases of meningitis occurred among 3,566 patients less than five years of age. Patients aged five to nine years numbered 5,539, 32 per cent of all patients with scarlet fever, but this group included fifteen, or 79 per cent, of those with meningitis. Since only one of the patients with meningitis was in the second decade, and one in the age-group twenty to twenty-nine years, the frequency was less than would have been expected from the number of cases of scarlet fever in those age groups.

The distribution according to sex (eleven males and eight females) was in agreement with that for scarlet fever, in which the number of males is slightly in excess of the number of females.

The seasonal distribution was like that of scarlet fever in this locality, with the greatest number of cases in late winter and early spring and an annual peak of incidence in April and May. Sixteen of the meningitis cases were in the first six months of the year, the time when scarlet fever is most common and complications referable to the nose and the ear most frequent.

Four patients presented initial symptoms of meningitis within ten days after the onset of scarlet fever, and six, between the eleventh and twentieth days. The interval for the other nine patients was more than twenty-one days. The longest interval was 117 days, the shortest, five days. The earliest reported onset of scarlatinal meningitis is on the fourth day[13] of scarlet fever.

Eleven of the nineteen cases of purulent meningitis followed septic scarlet fever. Three were in the course of moderately severe infections and five in the course of moderate scarlatina. Only 3.1 per cent of all patients had septic scarlet fever, but 58 per cent of those with meningitis were in this group. The frequency of meningitis among patients with mild scarlet fever was 0.05 per cent, and among patients with septic infections, 2.0 per cent. It is generally appreciated that all complications are more frequent with septic scarlet fever than with milder forms although, of course, the severest complications can follow the mildest of original infections.

Meningitis was invariably secondary to a primary focus of infection, usually adjacent to the meninges but sometimes remote. Thirteen cases occurred after suppurative otitis media and four through extension of infection from the paranasal sinuses. In two instances, meningitis followed intermediate hematogenous distribution of the streptococcus from a local wound.

INVASION OF THE MENINGES

Infection of the meninges from the primary focus is either by way of the blood or lymph stream or by direct extension from adjacent structures. Meningitis of scarlet fever developing without a preceding suppurative complication has occasionally been reported. Forbes,[7] commenting on a primary case without otorrhea, admitted the possibility that postmortem examination would very likely have shown an intermediate focus of infection in the middle ear and felt that primary cases of scarlatinal meningitis would doubtless be reported less frequently if greater care were exercised in determining sources of infection at necropsy.

In a discussion of nasal paths of infection, Hajek[14] considered that the usual process involved a spread of infection by tissue continuity through bone and dura and subsequent dissemination either by blood stream, by lymph stream, or by lymph channels along the olfactory nerves. Turner and Reynolds[15] studied twenty cases of nonscarlatinal streptococcus meningitis originating from nasal infections. For eighteen the path of infection was traced through the osseous wall of chronically inflamed frontal (five), ethmoid (six), and sphenoid (seven) sinuses.

Invasion by way of the nasal accessory sinuses was responsible for four of the nineteen infections of the meninges in our group of patients with scarlet fever. Two also had an abscess of the frontal lobe of the brain without localizing signs. Headache and photophobia were outstanding symptoms. A typical example is presented.

CASE 1.—Patient E. C., aged twenty years, became ill on Jan. 31, 1932, with complaints of severe frontal headache, tenderness referable to the eyes, moderate photophobia, and lacrimation. She developed sore throat, vomiting, fever, and headache on February 2. A typical scarlatiniform rash appeared on February 4. The usual evidences of moderately severe scarlet fever, together with bilateral conjunctivitis and slight edema of both eyelids, were present at the time of admission to the hospital, February 5. The areas over both maxillary sinuses were swollen. The maxillary swelling rapidly subsided, but infection of the ethmoid cells so progressed that the right eye was pushed forward and both eyelids became markedly edematous. The frontal headache, present since onset, increased progressively. The temperature on the first day in the hospital was 101° F.; the pulse rate, 128; and respirations, 28 per minute. During the next three days the fever slowly but progressively increased to 102° F. A direct transfusion of 400 c.c. of whole blood was given on the tenth day with no appreciable effect on the fever or improvement in the condition of the right eye. Examination disclosed a stiff neck and a positive Brudzinski sign. The headache increased in severity. There was a left lateral nystagmus. The swelling above the right eye increased and the area over the right frontal sinus was exquisitely tender. The deep tendon reflexes could not be obtained; the Babinski and Kernig signs were positive. The cerebrospinal fluid was turbid and contained 8,000 cells per c.mm. of which 90 per cent were neutrophiles. The test for globulin was positive. Microscopic examination showed many gram-positive cocci in chains. Hemolytic streptococci were identified in subsequent cultures. Death occurred on the thirteenth day of scarlet fever, fifteen days after the acute upper respiratory infection which immediately preceded the onset of scarlet

fever. The significant features at necropsy were abscess of the right frontal lobe, right purulent ethmoiditis, and generalized purulent leptomeningitis (Chart 1).

In agreement with secondary meningitis generally, scarlet fever streptococcus meningitis was noted more frequently after otitic infection than after paranasal sinus disease. Thirteen instances of purulent meningitis occurred among 2,925 patients with scarlet fever and otitis media 380 of whom had surgical mastoiditis. Six cases developed relatively early in scarlet fever, between the second and third weeks, while seven were late in the disease, from the fifth to the seventeenth week. In the following case otitis media appeared on the seventh day of scarlet fever, operation for mastoiditis on the fortieth day, and meningitis on the sixty-second day.

CASE 2.—Patient E. Z., a girl five years old, had a tonsillectomy on January 13. A generalized scarlatiniform rash appeared on January 16, and the family physician diagnosed the illness as scarlet fever. On admission to the hospital January 21,

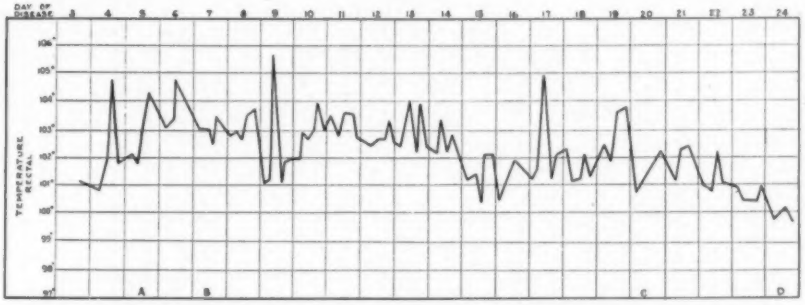

Chart 1.—(Case 1). Pansinusitis and meningitis in scarlet fever: *A*, moderate scarlet rash, edema of eyelids, severe headache; *B*, early pansinusitis serosanguineous discharge from nose, persistent severe headache; *C*, purulent meningitis; *D*, death.

examination revealed a moderately ill child with a branny desquamation of the skin. The tongue had enlarged papillae and was completely peeled, corresponding to scarlet fever of about a week's duration. The pharyngeal mucous membrane was reddened, and the tonsillar fossae were covered with grayish white exudate. The surgical procedure nine days previously presumably accounted for this condition. The temperature was normal. A sharp rise in temperature to 102.8° F. occurred the next day, due to development of bilateral catarrhal otitis media and enlargement of a left cervical lymph node. The inflammation of the gland subsided within a few days, but the left ear began to discharge pus. The temperature did not return to normal until the twentieth day of illness. Subsequently the purulent discharge from the left ear diminished, and the clinical conditions became satisfactory. On the twenty-sixth day there was fever of 103° F. accompanied by an increased amount of purulent discharge from the left ear. This continued to be more or less profuse during the next two weeks, and there was always more or less fever. Complaint of pain related to the ear occurred several times when the discharge from the ear became scanty. On the thirty-eighth day pain was first noted over the left mastoid process. This became increasingly more severe, and left mastoidectomy was performed on the fortieth day. Postoperative convalescence was satisfactory in that the temperature receded to normal within four days and remained essentially so

for the succeeding ten days. On the fifty-fifth day the temperature rose abruptly, and the patient again complained of pain in the left ear. On the morning of the sixty-second day the patient was listless and drowsy and complained of a severe frontal headache. Vomiting was a distressing symptom. Neurologic examination was essentially negative except for sustained left ankle clonus. Lumbar puncture revealed a cloudy fluid under normal pressure. Cultures served to demonstrate hemolytic streptococci. Spinal drainage followed by intrathecal administration of polyvalent streptococcus antibacterial serum and streptococcus antitoxin was performed each day, but death occurred three days after the onset of meningitis. Necropsy disclosed a generalized purulent leptomeningitis (Chart 2).

Streptococcus meningitis of hematogenous origin from a remote focus is uncommonly rare. A case reported by Scholle[16] followed a sup-

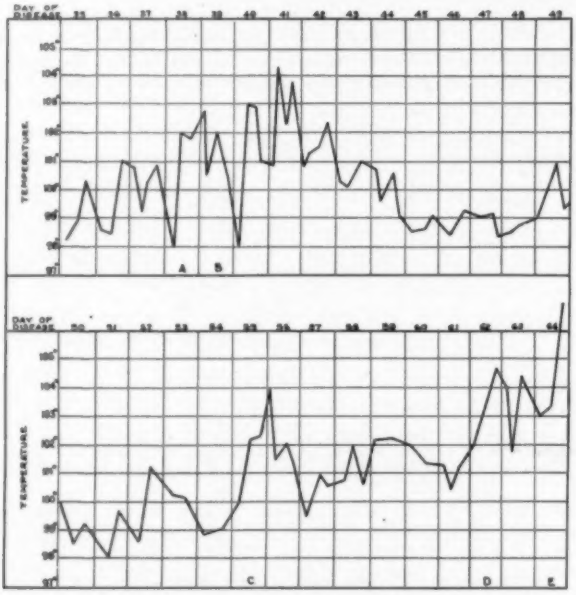

Chart 2.—(Case 2). Otitic meningitis following moderate scarlet fever: *A*, left mastoiditis; *B*, mastoidectomy; *C*, pain in left ear and mastoid; *D*, purulent leptomeningitis; *E*, death.

purative knee joint. Another patient[17] convalescent from scarlet fever sustained a head injury and developed clinical meningitis, confirmed by autopsy. Suppuration in a joint was the primary source of infection in two case of this series. The first case was unusual in that traumatic injury of the knee preceded scarlet fever by ten days. There was localized infection in the joint, septicemia, and subsequent meningitis. The other patient had an infection of the joint on the fourth day of ordinary scarlet fever with generalized infection on the fifth day, of which meningitis was a part.

CASE 3.—Patient R. S., a boy seven years old, was admitted to the hospital March 21, four days after the onset of scarlet fever. The eruption of the skin was well pronounced and typical of scarlet fever. The temperature was 102.4° F.; the pulse rate, 140; and the respirations, 32. About two weeks previously the patient had injured his left knee in a fall. One week later, three days before the appearance of the rash of scarlet fever, the knee and the entire leg became red and swollen. Shortly after admission to the hospital, curettement and free drainage for osteomyelitis showed much pus beneath the periosteum of the upper half of the tibia and necrosis throughout the length of the bone. The fourth day thereafter the patient was irritable, complained of headache, and toward evening was delirious. The next day the fever was 104° F.; the patient was irrational and had stiffness of the neck. The cerebrospinal fluid contained 1,080 cells per c. mm., mostly neutrophiles, and numerous hemolytic streptococci. Repeated lumbar and cisternal punctures, with administration of scarlet fever streptococcus antitoxin, were without benefit. Death occurred two days later, ten days after the onset of scarlet fever. Toxins were prepared from strains of hemolytic streptococci isolated from the wound, the throat, and the cerebrospinal fluid. All were neutralized by scarlet fever streptococcus antitoxin, determined by skin test (Chart 3).

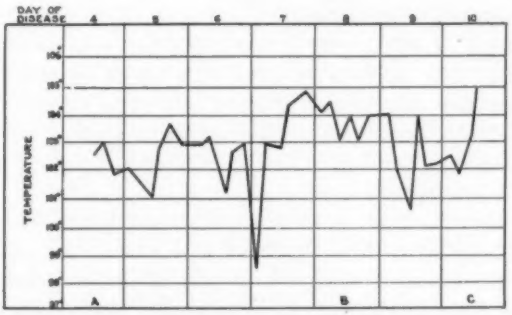

Chart 3.—(Case 3). Acute osteomyelitis of upper end of left tibia and septic scarlet fever; *A*, incision and drainage of left tibia; *B*, purulent meningitis; *C*, death.

Clinical Diagnosis.—Few difficulties attend the clinical determination of frankly active meningitis. The rapidly developing illness, the altered physical signs from meningeal irritation, and the changes in the cerebrospinal fluid are prominent developments. The clinical patterns in the course of scarlet fever which suggest the possibility of impending meningitis are not as readily evident. Early surgical drainage of the primary focus of infection will be emphasized as the first requisite in the management of the actively developed condition. An appreciation of the kinds of infection and the successive train of clinical events which precede meningitis can indicate the need for operation under circumstances that might otherwise not be considered pertinent.

Secondary rhinitis and sinusitis are common late complications of scarlet fever but are singularly unattended by serious consequences. Scarlatinal meningitis of nasal origin has been invariably related in this experience to profuse purulent or seropurulent nasal infections

that develop coincidentally with the onset of the disease. The general illness corresponds to that form of scarlet fever described as septic. Pansinusitis is almost always present. Acute suppurative ethmoiditis, with swelling of the eyelids and broadening of the root of the nose, is of serious moment and should suggest the danger of meningitis. If the swelling is localized at the inner canthus of the eye, the condition may appear more alarming, but the danger of meningitis is less since this indicates localization of the infection rather than extension. Lack of such localization, developing proptosis of the eye, increasing tenderness over the other sinuses, particularly the frontal, and complaint of extreme persistent headache with fever that lasts without remission for much more than five days are signs which indicate extension of the infection toward the meninges. In scarlet fever, meningitis after sinus infection is usually an early development; after otitis media, a late one. Progressive drowsiness with increased fever is a fairly certain indication of meningeal infection. Lack of response of the abdominal reflexes is one of the earliest physical signs; another is tenderness of the neck which often precedes actual rigidity.

The likelihood of meningitis in otitic conditions is more difficult to determine than with sinus infections. The condition can appear suddenly, without warning. As a matter of cold experience, we have more than once entered a ward on a given morning to find a patient with definite meningitis, the suspicion of which had not even remotely been suggested the previous day.

A person who has once had otitis media and later contracts scarlet fever is not only more likely to have a second attack of middle ear disease but in our experience presents more than the usual probability of mastoiditis with intracranial complications. Mastoiditis after septic scarlet fever offers, in general, a greater possibility of secondary meningitis compared with the original infections of the mild toxic form.

An apparently benign otitis media with a normal temperature or low-grade fever, but with periodic rises accompanied by decreased purulent discharge, warrants serious attention. Tenderness over the mastoid process may be absent or indefinite. The mildness of the symptoms and the brief duration of the exacerbations suggest a conservative attitude toward mastoidectomy. Such conditions are potentially dangerous and operation should be performed with less than the usual indications.

Otitis media with progressively developing and definite infection of the mastoid cells presents far less danger in respect to intracranial complications. Mastoiditis with marked swelling over the mastoid process or anteriorly over the zygomatic cells, with edema of the superficial tissues, protrusion of the ear, much pain, much swelling and even subperiosteal abscess formation is likely to end well with adequate surgical management. There is evidenced a tendency toward localization, and the condition is comparable to the paranasal sinus infection which points

outward. A slowly developing but long-continued infection which tends to progress centrally without alarming fever, with little or no swelling or tenderness about the mastoid region and with indefinite constitutional reaction, is cause for far more apprehension.

Meningitis in scarlet fever can occur as an aftermath of septicemia from a remote focus but commonly does not. Usual secondary localization in hemolytic streptococcus septicemia of scarlet fever is in the soft tissues of the body with formation of abscesses. Less commonly, resolution occurs through localization in the joints, in bone, or in both hard and soft parts. Many instances of prolonged septicemia have been encountered in this series, but only two terminated in meningitis. The interval between septicemia and meningitis was in both instances brief.

FATALITY OF SCARLATINAL MENINGITIS

A favorable outcome is infrequent with secondary meningitis of any sort. It is particularly uncommon with hemolytic streptococcus meningitis. In 1931 Rosenberg and Nottley[18] collected records of forty-one patients who had recovered from nonscarlatinal hemolytic streptococcus meningitis. Appelbaum[19] in 1932 found two additional cases and added three of his own. These reviews did not include one recovery reported in 1927,[6] three[12, 20, 21] in 1930, and three[22-24] in 1931. The literature of 1932 contains seven,[25-30] and three[31-33] appear in 1933; consequently, in all there are now on record sixty-three recoveries from streptococcus meningitis. The number of unreported recoveries can only be conjectured but probably is not great because recovery from this malady is uncommon enough to suggest reporting. Among the sixty-three patients with streptococcus meningitis who recovered, six[6, 8-10, 12, 34] had scarlet fever streptococcus meningitis. With one other case reported here, the number of reported recoveries from scarlet fever meningitis is seven, and for all streptococcus meningitis, sixty-four.

CASE 4.—Patient L. M., a boy aged five years, was admitted to the hospital Mar. 18, 1928, on the third day of scarlet fever, the temperature being 101° F., the pulse rate 100, and respirations 22. The next day the fever was 101° F., and both tympanic membranes were injected, the left bulging moderately. One therapeutic dose of scarlet fever streptococcus antitoxin was administered intramuscularly. Paracentesis of the left ear drum was performed March 20, with profuse discharge of pus. The temperature the next day was still about 104° F., and toward evening the patient appeared listless. The neck was moderately stiff. On March 22 the general clinical condition was poor; the patient was semicomatose, and there was first noted redness and moderate swelling over the left mastoid. The Kernig, Brudzinski, Babinski, and Oppenheim signs were readily demonstrated. The deep tendon reflexes were absent; bilateral ankle clonus was demonstrated. The cerebrospinal fluid was cloudy, containing 1,820 cells per c. mm., with 80 per cent neutrophiles. Streptococci were obtained by bacteriologic examination of the fluid. The patient became rational after the lumbar puncture and seemed improved. Scarlet fever streptococcus antitoxin with polyvalent antibacterial streptococcus serum was given intravenously and subsequently repeated twice. Three

lumbar punctures during the next five days showed a decrease in the number of cells to 275, then 110, and lastly 20. Neutrophiles predominated in the first two fluids, lymphocytes in the third. The opposite (right) ear meanwhile had started to drain spontaneously. The general clinical condition of the patient had been such that mastoidectomy was beyond consideration. On April 4 general improvement of the meningeal condition was such that bilateral mastoidectomy was chanced although the surgical risk was not good. The outer table of the bone was firm, but behind it free pus was found with extensive destruction of the inner plate. No sinus or dural exposure was necessary. The fever receded to normal April 9. Because of unsatisfactory progress, the mastoid wounds were reopened on April 23, a needle was inserted through the dura on the right side and much fluid under increased pressure was released. The brain substance in this area lacked normal consistency. Infected bone was removed from the left mastoid. Convalescence was subsequently uneventful. The patient was dismissed after seventy-nine days in the hospital. Two years later he was still in good health (Chart 4).

Another patient with suspected but unproved secondary meningitis was also encountered in these observations. Recovery followed. The low

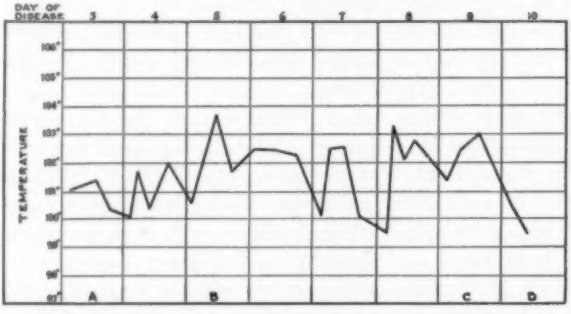

Chart 4.—(Case 4.) Septic scarlet fever: *A*, suppurative otitis media; *B*, left mastoiditis, purulent meningitis; *C*, bilateral mastoidectomy; *D*, convalescence, ultimate recovery.

sugar content of the cerebrospinal fluid suggested an infectious origin, but this was not substantiated bacteriologically. The condition has been interpreted as serous meningitis, and the case is not included in this series. It is reported because of its singular interest.

CASE 5.—A girl, six years old, was first seen on the fifth day of moderate scarlet fever. On the thirteenth day both middle ears discharged pus spontaneously, unattended by fever and without objective evidence of mastoid infection. In the fourth week the temperature increased; drainage from the infected ears was greater, but with no swelling or tenderness in the region of the mastoid process. On the thirty-sixth day of illness the patient was drowsy, irritable, with all of the classical signs of generalized meningeal infection. The cerebrospinal fluid was under pressure, and contained 1,080 cells, predominantly neutrophiles. No infectious agent could be demonstrated microscopically or by culture. Shortly thereafter, 250 c.c. of whole blood was given by transfusion from a person recently recovered from scarlet fever, and 2 c.c. of streptococcus bacteriophage was injected intramuscularly, and 5 c.c., intravenously. Three hours later bilateral mastoidectomy was performed; that evening lumbar puncture was repeated with injection of 5 c.c.

of bacteriophage intrathecally. Intrathecal injections of bacteriophage were repeated twice on the second day and twice on the fourth day; intravenous injections, in amounts of 10 c.c. on the second and fourth days. Thorough drainage of cerebrospinal fluid preceded each intrathecal injection. The number of cells did not exceed 1,670 per c. mm. No infectious agent could be demonstrated although all fluids were examined. The sugar content of the cerebrospinal fluids was decreased

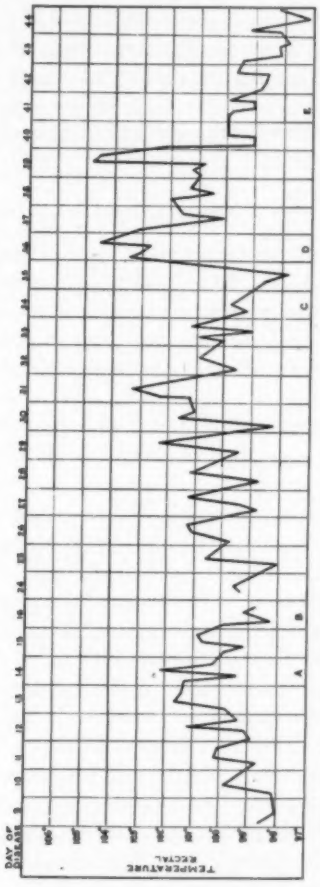

Chart 5.—(Case 5.) Moderate scarlet fever: *A*, otitis media; *B*, nine-day interval, normal temperature, free drainage from both ears; *C*, moderate bilateral mastoid tenderness; *D*, purulent meningitis; *E*, convalescence, ultimate recovery.

to 30 mg. per 100 ml. Immunotransfusion was repeated on the third day of meningitis. Ptosis of the left eyelid and strabismus were the only new clinical signs. There was progressive clinical improvement, and the temperature declined. After the fifth day, meningeal irritation was less marked, and the temperature did not exceed 100° F. Convalescence continued uneventfully, and the patient was released from the hospital on the eighty-fourth day of illness. Six weeks later there was no evidence of cranial nerve palsies, and recovery was apparently complete. No clinical evidence is lacking that this was an instance of generalized meningitis after scarlet fever. Bacteriologic identification of an infectious agent was not ac-

complished. Cultures of the aural discharge and from the mastoid wound contained hemolytic streptococci. It is interpreted as serous meningitis, although an infectious origin is possible (Chart 5).

The interval between the onset of meningitis and death is usually brief. Fourteen patients in our series expired within five days, and none survived more than nine days, other than the one who recovered. This short clinical course makes early institution of therapeutic measures essential if any benefit is to be expected. Kolmer has repeatedly emphasized the need for immediate early and adequate treatment, even drastic measures. An apparently unalarming clinical condition or a rational state at the onset of the condition does not permit delay because the course is invariably rapid.

TREATMENT

No specific therapeutic measure, nor even a satisfactory symptomatic method of management, has been developed for scarlet fever streptococcus meningitis. Antistreptococcus serums or chemotherapeutic agents do not compare in efficiency with the measures available for Type I pneumococcus meningitis, disappointing as they often are in that condition. Therapeutic suggestions are almost as numerous as the number of patients who have recovered. Many times a number of methods have been used in an individual case, thus making evaluation of any one impossible.

Accepted opinion is in agreement on the value of free drainage of the cerebrospinal fluid, through relieving symptoms due to pressure. Lumbar puncture is the commonest method, but of late cisternal puncture has often been practiced. The two may be alternated to advantage if the cerebrospinal fluid tends to become thick or organized through deposit of fibrin. Cisternal-spinal lavage with physiologic salt solution is of value under such circumstances. Various antibacterial streptococcus serums and scarlet fever streptococcus antitoxin have been administered intrathecally. Newer methods include the injection of Pregl's solution of iodine into the carotid arteries,[26, 35-37] usually combined with drainage of the cerebrospinal fluid by cisternal puncture; surgical drainage of the infected meninges by trephine or laminectomy;[38-43] and various chemotherapeutic agents[18, 35, 36, 44] administered intrathecally with the purpose of sterilizing the cerebrospinal fluid.

The intrathecal administration of either antibacterial or antitoxic streptococcus serums has in our experience proved disappointing. Neal[8] has seen two patients recover. The intracarotid injection of Pregl's solution of iodine or of serums, originally recommended by Kolmer,[35] has produced no demonstrable results. Nine patients with nonscarlatinal streptococcus meningitis and one with meningitis after scarlet fever were treated by this method. Ersner and Mendell[26] have recently reported two recoveries.

The methods of management used with this group of patients are presented in Table I. One patient recovered (Case 4). Polyvalent antibacterial and antitoxic streptococcus serum was administered intravenously, combined with daily drainage of cerebrospinal fluid by lumbar puncture (Table I).

TABLE I

METHODS OF MANAGEMENT IN SCARLET FEVER STREPTOCOCCUS MENINGITIS

CEREBROSPINAL DRAINAGE	THERAPEUTIC AGENT	ROUTE	CASES	DEATHS	RECOVERIES
Lumbar puncture	None	----------	6	6	
Lumbar puncture	S. F. Strep. antitoxin and polyvalent antibacterial serum	Intravenous	1		1
Lumbar puncture	S. F. Strep. antitoxin	Intraspinal	2	2	
Lumbar puncture	Polyvalent strep. antibacterial serum	Intraspinal	3	3	
Lumbar puncture	S. F. Strep. antitoxin	Intraspinal	1	1	
	S. F. Convalescent serum	Intramuscular			
Lumbar puncture Cisternal puncture	S. F. Strep. antitoxin	Intraspinal Intracisternal Intravenous	1	1	
Lumbar puncture Cisternal puncture	S. F. Strep. antitoxin polyvalent strep. antibacterial serum	Intraspinal Intracisternal	2	2	
Lumbar puncture Cisternal puncture	Polyvalent strep. antibacterial serum Immunotransfusion	Intraspinal Intracisternal	1	1	
Lumbar puncture Cisternal puncture	S. F. Strep. antitoxin Polyvalent strep. antibacterial serum Pregl's solution of iodine	Intraspinal Intracisternal Intravenous Intracarotid	1	1	
Lumbar puncture Cisternal puncture	Antistreptococcic bacteriophage Immunotransfusion	Intraspinal Intracisternal Intravenous	1	1	
Totals			19	18	1

The methods of management advocated by others and those which we have used permit but one conclusion, namely, that no single program of management exists which can regularly assure satisfactory results. None of the methods used has seemed to possess distinct advantages. Patients who recovered have been treated along widely dissimilar lines. From this experience with nineteen cases of scarlet fever meningitis and a larger group with nonscarlatinal streptococcus meningitis (sixty-nine cases), certain general principles can be emphasized.

Perhaps the most important, and certainly the first consideration, is to determine the original focus of infection. This is sometimes difficult, and again is impossible, to attack surgically. However, most infections of the leptomeninges in scarlet fever are secondary to middle ear disease, in which operative measures may aid materially.

The second consideration involves attempted sterilization of the cir-

culating blood. Meningitis may uncommonly be due to hematogenous infection. Much more frequently general sepsis is associated with meningitis, in which actual infection has been due to direct extension of infection from a local suppurative focus. The favorable results with immunotransfusion[45] in septicemic states of scarlet fever have influenced us to use that procedure when meningitis of scarlet fever is accompanied by streptococcus septicemia. That is not uncommon. Half of the patients had cultures of the blood containing hemolytic streptococci. Whole unaltered blood is given by transfusion from a patient recently recovered from scarlet fever.

Only after consideration of these two principles should attention be directed toward active treatment of the infected meninges. Repeated drainage of the spinal subarachnoid spaces is distinctly of value. This should be done daily; if necessary to relieve pressure, twice daily. The injection of antibacterial streptococcus serums and scarlet fever streptococcus antitoxin intrathecally has seemed to us to favor organization of exudate on the infected subarachnoid membranes to such an extent that actual blockage of circulation is not uncommon. Of late we have largely restricted measures to drainage combined with injection of air.

Streptococcus bacteriophage has been employed intrathecally in two cases, one, the unsubstantiated case (Case 5) with recovery, the other without demonstrable effect. We have been frankly skeptical of any value of these preparations in the treatment of infections. The clinical evidence is decidedly conflicting. Evans[46] contends that when bacteriophage comes in contact with body fluids, cells, or tissue débris, the lytic principle is inactivated. Kolmer and Rule[47] have recently treated experimental meningitis of rabbits by intracarotid injection of antistreptococcic bacteriophage. About one-third of the animals recovered.

SUMMARY

Purulent leptomeningitis is a very uncommon complication of scarlet fever. It is one of the commoner intracranial complications which are particularly rare in this disease. Of 17,311 consecutive hospital patients with scarlet fever, nineteen patients had generalized streptococcus meningitis.

Most instances of streptococcus meningitis originated from primary infection of the middle ear (thirteen); infected paranasal sinuses were a less common source (four); and two originated from localized suppurative infection of a joint, with subsequent hematogenous dissemination to the meninges.

The case fatality rate for scarlet fever meningitis is high. Only one of the nineteen patients in this series survived. Among the many patients reported by others in the course of years, only six are known to have recovered; seven in all.

No known therapeutic measure offers much promise. The prin-

ciples of management include removal of the original source of infection, attempted sterilization of the blood stream because general sepsis is often associated, and finally attempted sterilization of the infected meninges.

Repeated drainage of the cerebrospinal fluid is a worth-while procedure. Intrathecal administration of antistreptococcic serums and various chemotherapeutic agents has been disappointing.

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CONSTIPATION IN CHILDREN: ITS EFFECTS UPON BODY MECHANISMS

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THE ills ascribed to an infrequent or inadequate emptying of the bowel have been many and varied. A casual survey of different textbooks on gastroenterology lists the following conditions which may at different times be more or less closely identified with constipation: vertigo, frontal headaches, neuritis, insomnia, bad dreams, inability to concentrate, hysteria, infantile convulsions, and other nervous phenomena. It is also stated that individuals suffering from chronic constipation not infrequently have a furred tongue, bad taste, foul breath, gaseous eructations, poor appetite, colicky pains, cold extremities, sallow complexion, skin affections, anemia, cardiac palpitation, and albuminuria. It still seems to be the opinion of some physicians and a majority of the lay public that an inadequate bowel evacuation can be the sole cause of fever and that an increased body temperature can be brought to normal by an enema or an active cathartic.

In our experience, limited entirely to infants and children, the causal relationship of such states as those described above to constipation has always seemed far-fetched; a careful study of the patient has usually revealed a more definite etiologic factor, and this statement is especially true of the relationship attributed to convulsions or fever and constipation.

The purpose of this paper is to record the observations in seventeen children in whom an evacuation of the bowel was either absent or inadequate during the course of a number of days. Twelve of these children were normal physically at the onset of the experiment, while the remaining four were suffering from some fever-producing disease at the onset and during the course of the experiment. Each child was first carefully observed during a control period of five days, a record being made of the temperature and pulse rate every two hours, the normal appetite, and mental state; laboratory studies during this period included a full blood count, sedimentation rate, blood chemistry and urine examination. When these data were obtained, constipation was brought about by the use of the deodorized tincture of opium, all other controllable factors in the child's diet and environment remaining unchanged. The observations reported above were then continued, the blood examinations being repeated every sixth day.

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The ages of the children studied varied between four and twelve years, the majority being in the older group. At the onset of the experiment, twelve of these children had apparently completely recovered from the infection which brought them to the hospital and had normal temperature for at least ten days or more. Nine of these children had originally been hospitalized for acute respiratory infections; three had suffered from rheumatic fever; and one, at the time of admission, had infectious jaundice. All of the four children who still were acutely ill and febrile at the onset of the experiment were suffering from rheumatism and rheumatic carditis.

The number of days during which the effects of constipation were observed varied; the shortest period of observation was sixteen days; the longest, sixty-eight days; the average period of observation for the sixteen cases was thirty-six days. Complete obstipation was never obtained; every one of the subjects passed one or more small, hard, dry tools during the course of the experiment. On the average, each child had one small bowel movement once in every eleven days; however, two children went over twenty-five days without any evacuation, one being completely constipated for twenty-nine days. It is interesting to note that to bring about these results large doses of a potent preparation of the deodorized tincture of opium were necessary; constipation usually was not obtained until the child received 30 minims daily, and at times as much as 75 minims daily were necessary. No untoward results were observed from the administration of what was formerly thought to be such a large dosage of an opiate for a child.

The children almost all appeared comfortable and happy during the course of the experiment. There was no complaint of headache, lassitude, bad taste, gaseous eructations, or other symptoms commonly associated with constipation. Their appetites may have been slightly decreased although this is a difficult factor to determine. However, as a group they gained 18 pounds during the course of the experiment, or a little over 1 pound per child. (This weight was recorded at the completion of the experiment, after the bowel had been thoroughly evacuated.) Many children did complain of some pains about the anus while passing a hard dry constipated stool, and two of the older children had some lower abdominal discomfort toward the end of the experimental period; both of these children were twelve-year-old girls, who had been made conscious that they were being artificially constipated; this may have played a factor in their mental attitude and symptomatology.

An analysis of the objective findings of this group is as follows:

Temperature.—No effect whatsoever could be noted. In ten of the twelve children with normal temperatures at the onset of the experiment, the temperature continued unchanged throughout. In two children there was a rise in temperature caused by an intercurrent upper

respiratory infection, one of whom had fever ranging between 102° and 104° F. for three days and the other, between 100° and 103° F. for five days; in both of these children the period of constipation was continued during the course of their infection and for many days thereafter; and in both of these cases with the subsidence of the infection, the temperature dropped to normal and continued so thereafter.

In the four children who were febrile at the onset of the experiment, no definite difference in the temperature curve could be noted while the experiment was in effect. When the period of constipation was stopped and an enema and cathartic administered, there was also no change from the regular fever curves previously noted.

The pulse rates were similarly unaffected.

Blood Count.—Here also no definite changes were observed, the constipation apparently having no effect upon either the hemoglobin, the red cell count, the white cell count, or differential count. The average hemoglobin at the onset of the experiment was 82 per cent (Sahli) with 4,160,000 red blood cells. At the end of the period of constipation, the hemoglobin averaged 83 per cent and the red blood count 4,020,000.

Of the twelve afebrile cases, the average white blood count at the onset was 8,700 with 62 per cent polymorphonuclear cells, 33 per cent lymphocytes, and 5 per cent monocytes; included among the polymorphonuclear cells there were 2 per cent staff cells. At the end of the experiment the average white blood count was 8,400 with 60 per cent polymorphonuclear cells, 36 per cent lymphocytes, and 4 per cent monocytes, the number of staff cells remaining the same.

Sedimentation Rate.—The blood sedimentation rate was similarly unaffected by constipation, no appreciable change being noted at any time in either the afebrile or febrile cases.

Blood Chemistry.—Urea nitrogen, nonprotein nitrogen, and creatinine determinations were made in each case before, during, and at the end of the experiment. These figures remained normal and relatively unchanged throughout. In five cases the blood cholesterol was also determined; the average figures obtained at the onset of the experiment were 194 mg. per 100 c.c. of blood; at the termination of the period of constipation this average had risen to 204 mg. per 100 c.c. of blood, a slight change without any real significance.

Blood indican was determined in two cases; this also remained unchanged although the urinary indican increased considerably in the majority of cases. In one case at the onset of the experiment, the amount of indican recorded was 0.068 mg. per 100 c.c. of blood; after forty-two days of constipation during which time the child had three small, hard, dry stools, the figure changed to 0.062 mg. per 100 c.c. of

blood. In the second case the blood indican at the onset of the experiment was recorded as 0.062 mg. per 100 c.c.; at the end of fifty days of constipation during which the child passed four small stools, this figure had risen to 0.072 mg. per 100 c.c. of blood.

Urine.—No appreciable change except the appearance of a more or less heavy trace of indican in the majority of cases was noted during these examinations. One girl developed urinary frequency, probably due to the pressure of impacted feces in the rectum and lower bowel. This was relieved after a thorough evacuation of the bowel. No albuminuria was noted, nor was there any evidence of an increase in the white blood cells.

Basal metabolism determinations were made in two cases at the onset of the experiment and during the latter period of constipation without any appreciable change.

An x-ray examination of the gastrointestinal tract in three cases revealed a similar picture in all of them: normal gastric motility, gaseous distention of the small intestine, and a colon packed full of feces.

SUMMARY AND CONCLUSIONS

A study of sixteen cases of artificially produced constipation in twelve children who were well and in four who were subacutely or chronically ill revealed no definite changes, either from the subjective or the objective standpoint.

As far as could be determined from physical examination, temperature charts, complete blood analyses, and urinary examinations, no demonstrable changes occur in rather severe chronic constipation in children.

The temperature charts were especially striking. At no time could any rise in temperature be associated with constipation; in two children who developed definite acute respiratory infections and fever during the course of the experiment, the temperature subsided and then continued normal even though no bowel movement occurred during the illness and for many days thereafter. Furthermore, a thorough bowel evacuation at the end of the period of constipation produced no changes upon the average temperature curves in those children who were ill and febrile throughout the experiment.

Thus it can be said with a fair degree of certainty that an infrequent or inadequate bowel evacuation cannot experimentally be demonstrated as producing harmful effects in children.

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MASKED HYPOTHYROIDISM IN CHILDREN

Osseous Development as an Aid in Diagnosis

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A STATISTICAL analysis of a group of 500 children sent to the clinic for endocrine study revealed 15 per cent to be hypothyroid in a masked state. The presence of this condition in such a comparatively large number of children prompts the presentation of this protocol. It is hoped that the few cases to be presented here will add to the already mounting literature on the subject, especially to the arguments of Shelton[1, 2] and Cattell.[3]

The term "masked" is used to indicate a condition which offhand does not point to hypothyroidism and which therefore may go unrecognized unless carefully studied and interpreted. While the signs and symptoms of classic cretinism and marked hypothyroidism present an easily recognizable type, the picture of mild hypothyroidism often goes unrecognized because the complaints of the patient are misleading and often are misinterpreted.

In the cases to be cited, ordinary therapy administered for the complaints of the patient and not for the real cause, such as laxatives for constipation or ointments for eczema, brought little benefit. A thorough study of the past and present history was therefore made with the view of bringing to light other or more hidden symptoms, such as tardiness in walking, talking or teething, stunted body growth, genital hypoplasia, or poor mental response. These symptoms, in addition to the complaints enumerated by the patient, were the means of detecting the hypothyroidism. As will be seen in the cases to be cited later, not all of the symptoms listed above appeared in every case—often only one or two of these existed—but even only one or two of these were considered sufficient clues for further study. As early as 1913, Leopold-Levi and Rotschild,[4] Leopold-Levi,[5] and Hertoghe[6] associated several of the above clinical symptoms with a subthyroid state.

A final diagnosis of mild or masked hypothyroidism was based primarily on:

1. A history of either physical retardation or of mental retardation, or a combination of both.

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Presented before the New York Endocrinological Society, March 28, 1934.

2. The existence of signs and symptoms akin to the symptoms of the classic cretin or marked hypothyroid; however, these symptoms were apparent in a much milder degree.

3. The presence, in a varying degree, of delay in the unfolding of the osseous framework, as revealed by roentgenograms.

This latter condition, delay in the unfolding of the osseous framework, was carefully studied and was considered to be of definite diagnostic importance. Although the osseous development of the cretin, as revealed by the roentgenogram, has been studied for some time, the same study of the osseous unfolding has not been sufficiently considered for the recognition of the mild or borderline case. All children who presented any suspicion of hypothyroidism were subjected to a thorough roentgen ray study of the bony framework. The presence of any bony retardation as revealed by this study was accepted as confirmatory evidence of hypothyroidism, providing that rickets, mongolism, celiac disease, juvenile congenital syphilis, and Cooley's erythroblastic anemia were eliminated.

In those cases in which the hypothyroidism was of too recent onset to make osseous retardation roentgenographically apparent, a basal metabolic test was made whenever the child was old enough to cooperate. With children who were too young for a metabolic test and yet showed clinical evidence of a recent onset of thyroid insufficiency, thyroid medication was administered and was found to be efficacious. The recent observations of Topper[7] are of interest in this connection. She reported the effect of thyroid therapy on children selected because of retardation in mental or physical development, without an obvious defect in the function of their thyroid gland. The findings show that thyroid administration markedly stimulated the growth and development of these children even though in some cases the basal metabolic rate was normal. Dentition, mentality, growth in height, and osseous development were improved by thyroid therapy in those who showed evidence of retarded development. It is my belief that Topper's cases may have fallen under the classification of "masked" hypothyroidism, for, in addition to the findings of mental or physical retardation, these children suffered from osseous retardation which responded to thyroid therapy.

It must be pointed out that, while all of the cases in this series have been diagnosed as "masked" or mild hypothyroidism, other factors (at present not definite) may be responsible for the osseous retardation. Some of these conditions have been mentioned above.

RÉSUMÉ: MASKED HYPOTHYROIDISM WITH RETARDED OSSEOUS DEVELOPMENT

1. Incidence in a series of 500 cases referred for an endocrine study 15%
2. Number of cases in this series—40
   Males 60%
   Females 40%

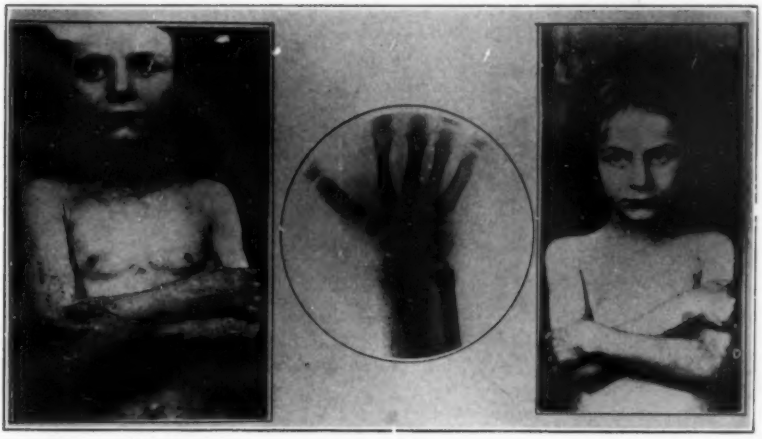
3. Familial	35%
4. Height	
Repressed height	60%
Normal range	25%
Accelerated height	15%
5. Weight	
Underweight	34%
Normal range	38%
Overweight	28%
6. Genital development (males)	
Normal testes	15%
Hypoplastic testes 45% Undescended testes 40% (unilateral or bilateral)	85%
7. Bowels	
Normal	44%
Constipated	34%
Sluggish	22%
8. Mentality	
Retarded	32.5%
Fair	27.5%
Good or bright	32.5%
Excellent	7.5%
9. Nervous and emotional tendencies	
Apathetic	25%
Unstable { irritable, bad stubborn, spiteful }	28%
Restless and poor sleepers	9%
Active and alert	38%
10. Skin	
Dry	50%
Normal	50%
11. Hair	
Dry or poor luster	65%
Normal	35%
12. Laboratory Findings	
Calcium (9 cases)—range 9.1 to 13.6 mg.	
Phosphates (5 cases)—range 4 to 6.5 mg.	
Cholesterol (6 cases)—range 100 to 210 mg.	
Basal metabolic rates (9 cases)	−23% to −4%

CASE 1.—A. M., a girl, aged six years eight months, was referred Apr. 12, 1932, with a history of dryness, itching, and hardening of the skin. This condition had persisted since she was six months old. Another child in the family also has a tendency toward this type of skin condition.

On examination it was found that the patient weighed 41 pounds (average normal, 40.7 to 50.8) and was 45 inches tall (average normal, 44.7 to 47.8).[8] There was marked dryness, toughness, and scaling of the skin with scratch marks and excoriations. The skin was wrinkled, leathery, and thick over most of the body. The hair was dry, sparse, and lusterless. The facies, presenting a prominent forehead and somewhat widely spaced eyes, was slightly suggestive of the cretinoid type. The patient, apparently, was not dull but not very cooperative. The basal metabolic rate was minus 14 per cent (test fairly satisfactory). Roentgenograms of the wrist and hands showed the presence of seven small carpals.[9] The distal epiphysis

of the ulna was present but small. Since the patient was a female and showed poor massing, it was felt that she was from eight to twelve months retarded in bone development. In view of the above findings, a diagnosis of mild hypothyroidism together with a moderate degree of ichthyosis was made.

The patient was put on a standard brand of thyroid substance varying from 1 to 5 grains daily. She did not begin to show a response to treatment until after the larger doses were administered. On June 29, 1932, two and one-half months after the institution of this treatment, the following note was recorded, "Skin much improved and apparently taking on a moist feel; the hair has a better luster but is still dry; the skin is not wrinkled as previously, and is clearer." Prior to this time, according to the patient's mother, the skin had always been the same; there were no marked remissions, in spite of different ointments administered from time to time. On Feb. 28, 1933, the patient was examined again. At this time her condition was noted as satisfactory although the skin of the hands was still dry. A basal metabolic rate showed a plus 25 per cent. In April, 1933, one year after treatment was instituted, the height was 48 inches and the weight, 48 pounds (an increase of 3 inches, and 7 pounds). The patient discontinued visiting the clinic.



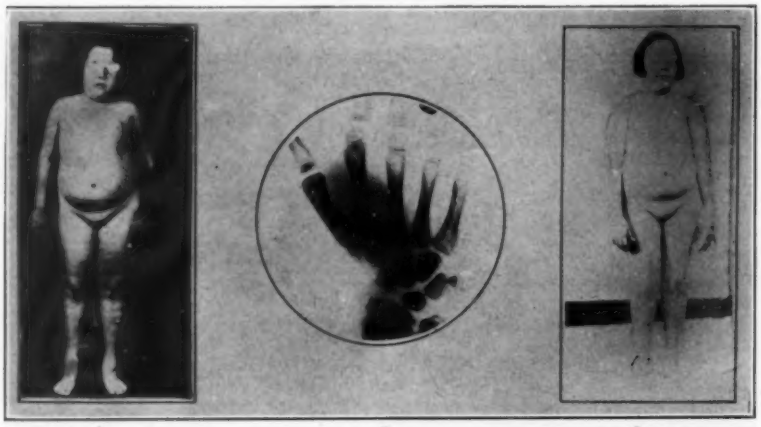
A. *B.* *C.*

Fig. 1.—Case 1. *A*, Patient at the age of six years and nine months, Apr. 20, 1932. *B*, Roentgenogram of bones of hand at same age, Apr. 13, 1932. *C*, Patient at age of seven years and three months, Nov. 22, 1932.

About one year later, Jan. 22, 1934, a visit was made to the patient's home. She was found to be generally well. There had been a gain in height and weight in spite of the fact that thyroid substitution had been neglected in the interim. The child had not had an acute exacerbation of her skin condition. However, casual examination showed a return of some of the dryness and leatherlike skin about the legs and knees, hands and forearms. The itching and excoriations had not recurred. Altogether her condition was much better than at the first examination.

Fox[10] believes ichthyosis to be a congenital malformation of the skin of unknown cause although certain facts point to an endocrine etiology. Porter,[11] however, associates ichthyosis with hypothyroidism. In his series of ten cases in children ranging from eight to twelve years of age, he found 70 per cent with a basal metabolic rate below normal,

10 per cent above normal, and 20 per cent normal. In his treatment of these cases he noted that those who derived the greatest benefit from thyroid administration were those with the lower basal metabolic rates, while those with the normal or above normal rates derived little benefit. Although Porter's suggestion of treating cases of ichthyosis accompanied by low basal metabolic rates with thyroid therapy is important, it is not always possible, as has already been pointed out, to obtain basal metabolic rates in younger children. In such cases it has been suggested that a study of the osseous development be made; and, if the bone study reveals osseous retardation, thyroid substance in large doses should be instituted. I have recently encountered a number of children presenting osseous retardation who are suffering from



A. *B.* *C.*

Fig. 2.—Case 2. *A*, Patient at the age of eight years, Nov. 22, 1932. *B*, Roentgenogram taken Nov. 25, 1933, patient aged nine years. *C*, Patient at the age of nine years and four months, March, 1934.

marked chronic eczema since early infancy. Thyroid substitution seems promising in a number of these.

Case 2.—Mu. S., a girl, eight years four months of age, was referred for obesity. The infantile history was not significant except that she started walking at fifteen months and then developed pertussis and stopped walking until the age of twenty-two months. She was said to have had a mild case of rickets. At the time of examination she presented a marked girdle obesity, a short neck and increased supraclavicular and nuchal fat paddings. The posture was poor; there was a lordosis, bilateral pes planis, and a markedly relaxed and protuberant abdomen. The skin of her face was puffy and somewhat thickened. Her hair and skin were not dry. The weight was 87 pounds (average normal, 47.6 to 59.2); the height was 48 inches (average normal, 47.5 to 50.9). The patient was an average student at school although she was said to be sluggish at home. She was severely constipated.

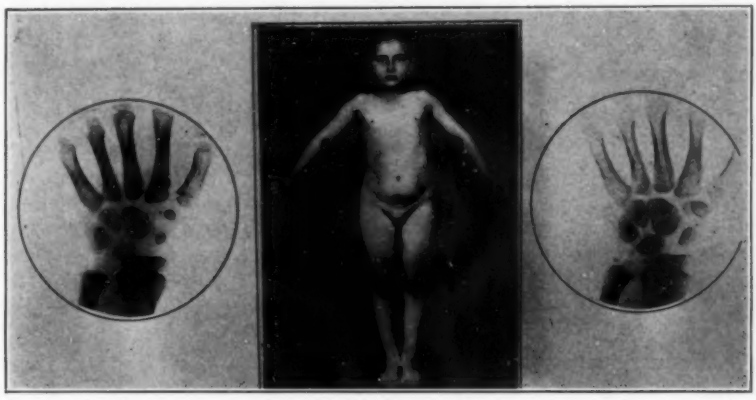
The basal metabolic rate was minus 14 per cent. Roentgenograms of her wrists and hands showed the presence of seven poorly massed carpal bones. The distal

ulnar epiphysis was present. There was a bone retardation of one year. A diagnosis of mild hypothyroidism was made.

Thyroid substance ranging up to 2½ grains per day was prescribed. Marked general improvement was noted. The facial expression became brighter; the patient became more alert; there was marked "thinning out" of the fat with a marked loss of fat in the nuchal and supraclavicular regions; the abdomen became less prominent.

At the end of ten months of treatment (at the age of nine years two months) the patient had gained 2⅛ inches in height and had lost 3 pounds in weight. Roentgenograms of the wrists and hands showed a better massing of the previously existing carpals, although these were still smaller than the average normal. The elbow showed an absence of the trochlea, the presence of which is normal at nine years. In all, she still showed a bone retardation of about six months.

CASE 3.—J. S., a white male child, seven years nine months old, had been treated in the general clinic since birth and was referred to the endocrine clinic for genital underdevelopment.



A. *B.* *C.*

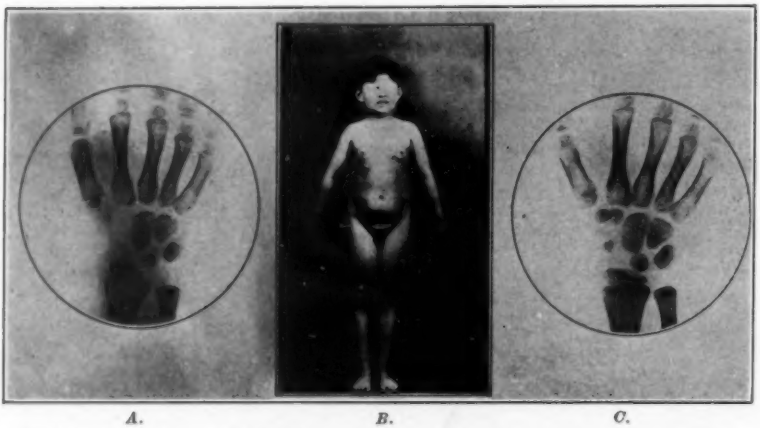
Fig. 3.—Case 3. *A*, Roentgenogram of bones of hand, patient seven years nine months old. *B*, Patient aged seven years six months, July 23, 1932. *C*, Roentgenogram of hand, Nov. 10, 1923 (patient aged eight years and nine months).

The patient's birth weight was 7¾ pounds. He cut his first tooth at ten months and started talking at an early age. He had received cod liver oil for a number of years, and his diet had been prescribed in the children's clinic. The patient had had no illnesses except mild upper respiratory infections and bronchitis. He was also said to have had bowing of the legs in early infancy. There was a slight eczematous condition of the face during his infancy.

Physical examination at the age of seven years nine months showed the weight to be 63.5 pounds (average normal 46.1 to 57.1), the height 46.5 inches (average normal, 47 to 50.3). The patient was obese. His hair was dry, lusterless, wiry, and stumpy. The left testis could not be felt, and the right testis was very small and retracted in the canal (these findings had been noted on the patient's record since the child was one year of age). At the age of four years the patient was examined by a surgeon who was able to pull down both testes but who said they were very small. Later, however, several careful examinations failed to reveal the presence of the left testis.

The basal metabolic rate was minus 14 per cent. The blood chemistry was as follows: cholesterol, 165 mg.; calcium, 13.2. The Wassermann reaction was negative. Roentgenograms of the wrist showed the presence of seven carpals, four of fair size and three very small. The distal epiphysis of the ulna was absent (present normally at six years). He was therefore retarded in osseous development from eighteen to twenty-four months. In view of the bone retardation, the lowered metabolic rate, the hypoplastic genitals, the obesity, the dry, stumpy, and lusterless hair, and the presence of a somewhat dulled mentality, a diagnosis of mild hypothyroidism was made.

Thyroid substance ranging from 1½ to 3 grains daily was administered for a period of one year. After this time there was marked improvement in his bone development; there being seven well-formed carpals in each wrist and a small distal ulnar epiphysis. The bone development, however, was still somewhat retarded. In addition to these findings his hair became fine, silky, and took on a good luster. Both testes, though small, had descended lower down the canal. The patient



A. *B.* *C.*

Fig. 4.—Case 4. *A*, Roentgenogram of bones of hand, patient aged seven years, Apr. 20, 1932. *B*, Patient at the age of seven years, May 2, 1932. *C*, Roentgenogram of bones of hand, Oct. 7, 1933, patient aged eight years and four months.

was brighter and more active and was less forgetful than previously. He had gained 3½ inches in height during the year of treatment.

CASE 4.—My. S., a white male child, seven years old, was referred because of undescended testes.

The patient's infantile history was normal as regards development. His birth weight was 8 pounds 11 ounces after a full-term normal delivery. He had had scarlet fever, measles, pertussis, and occasional colds. He had had and still was troubled by an eczematous rash behind the ears. It was felt by the mother that this came "after eating eggs." His diet was good and varied. The patient's parents were both very intelligent, and the boy's mentality was excellent, as evidenced by a good school record and extracurricular activities.

On examination (Apr. 19, 1932) the patient was found to be 49.5 inches in height (average normal, 45.6 to 48.8) and weighed 64 pounds (average normal, 43 to 53.2). There was slight girdle obesity. The teeth were normal; the hair and skin were not dry. The patient was troubled with chronic constipation. The testes were not felt except for a suggestion of a slight mushy mass in the left inguinal canal. The penis

was small. Blood analysis showed cholesterol, 165 mg.; calcium, 10.4; phosphorus, 5.2; fasting sugar, 95; creatinine, 1.2; urea nitrogen, 12. The urine showed a faint trace of albumin. The basal metabolic rate was minus 18 per cent. The bone development at seven years of age showed the presence of five small carpal centers in one wrist and six in the other. The distal epiphysis of the ulna was absent. Osseous development was retarded about twenty-four months. The sella turcica was normal.

The outstanding findings were moderate girdle obesity, cryptorchidism, slight periodic eczema, low basal metabolic rate, and retarded osseous development, all of which enabled a diagnosis to be made of mild thyroid insufficiency.

Thyroid substance ranging from 0.5 to 2 grains daily was administered. In addition to the thyroid therapy, the patient was placed for a short time on antuitrin and then on anterior pituitary-like hormone, 1 c.c. two to three times weekly hypodermically.[12] At the end of sixteen months of treatment he showed a filling out of the scrotum and the presence of two small pea-sized testes high up in the canal. A basal metabolic rate taken at this time was plus 1 per cent. The patient had also gained 3¼ inches in height during this period. Roentgenograms of his bones showed the presence of seven well-formed carpal centers instead of the five small ones formerly observed; however, the distal ulnar epiphyses were still absent. Osseous development was still retarded about ten to twelve months.

Stockard[13] emphasized that there is a great deal of evidence to show that the amount or quality of thyroid secretion present in the developing individual is an important factor in determining the rate of growth. The thyroid hormone affects the growth rate, primarily by determining or affecting the rate of metabolism.

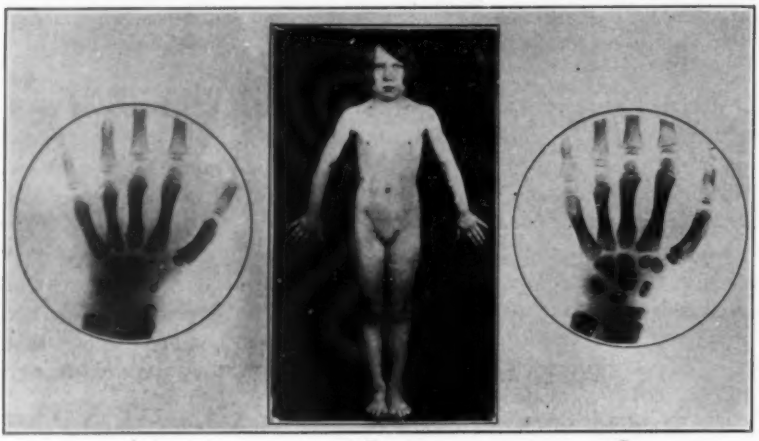
While it can be said that the majority of these patients are short in stature, it is apparent, as seen in the case reported above, that some of them fall within the average normal standards of height for their age in spite of an apparent thyroid insufficiency. It has been shown that there can be increased growth in thyroidectomized tadpoles even though differentiation as evidenced by metamorphosis is absent.[14]

The opinion is held that some cases of genital underdevelopment presenting undescended or hypoplastic testes, may be attributed to thyroid deficiency. Dorff[15] has reported a number of such cases showing retarded osseous development in addition to their underdeveloped genitals and is of the opinion that this genital hypoplasia in such children is secondary to a thyroid insufficiency. Thyroid substitution is of apparent benefit in this type of child. However, I believe that the anterior pituitary-like hormone supplementing the thyroid substitution enhanced the result in Case 4. It should be mentioned that thyroid substitution alone will stimulate definitely the hypoplastic genitals present in this type of patient although not nearly as rapidly nor as spectacularly as with the anterior pituitary-like hormone.[15]

Case 5.—G. T., a white female child, seven and one-half years of age, was examined in the general pediatric clinic on Apr. 1, 1932, because of small stature, dull mentality, dry hair, dental caries, and enlarged tonsils. She weighed 39 pounds (average normal, 44.1 to 54.9), and her height was 42.5 inches (average normal, 46.3 to 49.5). The diagnosis was infantilism, for which the patient was referred to

the endocrine clinic. It was reported that the patient was of a full-term normal delivery, the birth weight being 9 pounds. The first tooth appeared at eight months of age. She walked at one year and talked at the normal time. The patient was breast fed for eleven months and had not received cod liver oil until the age of three years. She had had measles and pertussis; she had suffered from occasional enuresis and constipation.

Blood analysis showed calcium, 13.6 mg.; fasting sugar, 125 mg.; nonprotein nitrogen, 36. The Wassermann reaction was negative. The urine showed a trace of albumin. The basal metabolic test was unsatisfactory. The intelligence quotient (Stanford-Binet) was 99; the examiner noted, "Child's manner leads me to believe she would do better on the performance type test." X-ray examination at seven and one-half years of age showed the presence of six carpal centers in one hand and seven in the other, of which only two were of fair size. The distal epiphysis of the ulna and the epiphysis for the head of the radius were absent (normally present at age of five years). There was bone retardation of twenty-four to thirty months. The sella turcica was normal.



A. *B.* *C.*

Fig. 5.—Case 5. *A*, Roentgenogram of bones of hand, patient aged seven years and six months, Apr. 9, 1932. *B*, Patient at the age of nine years and four months, Jan. 20, 1934. *C*, Roentgenogram of bones of hand, patient aged nine years and four months, Jan. 20, 1934.

A diagnosis of mild hypothyroidism was made, and 0.5 grain of thyroid substance daily was started. This medication was regularly taken for about six weeks and then discontinued by the patient. It was not until almost two years later, Jan. 18, 1934, that the patient was again presented. On this examination, after a two-year period without treatment, the objective symptoms were more pronounced. There were prominent thickened cretinoid features, with puffiness under the eyes; the skin and hair were dry and lusterless. There was a tendency to keep the mouth open and to protrude the tongue. The mother said the patient's responses were poor, that she forgot easily, and that she was slow in school. This latter fact was also mentioned at the first examination, although the patient was otherwise active. The mother thought that when the child took the thyroid substance she was much brighter. The patient's weight at this time was 44.75 pounds (average normal, 53 to 66), height 45.5 inches (average normal, 49.9 to 53.2). She had gained 3 inches in height and 5.75 pounds in weight in two years. Roentgen ray examination of the bones

(at age of nine years four months) showed some improvement over the original condition; there were seven carpals of fair size though these were definitely smaller and more poorly massed than in the average normal. The distal epiphysis of the ulna, the size of a pinpoint, was present. There was also retardation of the epiphysis at the head of the radius which was just appearing. Osseous development at this time was more retarded than at the first examination. The retardation was equivalent to about thirty-six to forty-two months. The sella turcica was normal.

This case illustrates several important points. A diagnosis of mild hypothyroidism was made two years previous to the administration of intensive thyroid treatment. The patient presented evidence of retarded ossification and other characteristics pointing to the diagnosis. At the end of two years the symptoms became much more pronounced, tending toward the cretinoid type, and, although her bone age advanced somewhat, it still lagged far behind the increment in her chronologic age. It was apparent that there was no spontaneous correction of the osseous retardation in this case.

Shelton's report[1, 2] of three siblings, all presenting retarded ossification, revealed that two of these siblings showed rapid carpal development and general somatic growth under thyroid therapy within a short period, while the third child, who received no treatment, advanced only slightly in bone age. In addition, the control patient also lagged far behind in the optimal increment in height and weight. It appears obvious then that such cases, incompletely treated, fall short of fulfilling their normal destiny.

SUMMARY

1. A series of forty cases from a group of 500 children submitted for endocrine study formed the basis of this report.

2. The mental or physical retardation, or both, in these children appeared akin to the same, but more severe, findings of sporadic cretinism and marked hypothyroidism.

3. This condition I would term "masked hypothyroidism" since the symptoms are misleading and often go unrecognized unless properly studied and interpreted. Careful questioning frequently discloses a chain of symptoms other than those of which the patient complains. When considered with poor somatic development and retarded osseous unfolding, the findings are significant.

4. Retarded osseous development may be evidenced by the late appearance or poor massing of ossification centers and epiphyseal nuclei. Such retardation was a most important factor in our diagnosis of hypothyroidism—mild as well as marked states.

5. In cases in which the hypothyroidism was of too recent occurrence to be demonstrated roentgenographically, other diagnostic measures were employed: in children over eight years of age, who were cooperative, a basal metabolic test was performed. If it was low, it

was considered as confirmatory evidence of hypothyroidism. In children under eight years of age, a basal metabolic rate was usually not informative.

6. Thyroid therapy was efficacious in cases in which, in addition to evidence of physical or mental retardation, there was (1) osseous delay, (2) a low basal metabolic rate, and (3) no response to other forms of treatment for the alleviation of the complaint or combination of complaints.

Acknowledgment is made to Dr. Mendel Jacobi, director of the pathology department of the Beth-El Hospital, for suggestions in compiling this report.

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1176 EASTERN PARKWAY

THE ANTIRACHITIC VALUE OF IRRADIATED EVAPORATED MILK IN INFANTS

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THIS investigation was made to determine the antirachitic value for infants of directly irradiated evaporated milk. The studies of Hess and Lewis[1] and Mitchell, Eiman, Whipple, and Stokes[2] indicated clearly that the vitamin D content of "fortified" milks determined by rat assay gave no clear indication of their clinical potency; thus Hess and Lewis found that directly irradiated milk, milk from cows fed irradiated yeast (so-called "yeast milk"), and viosterol, all containing the same number of rat units of vitamin D, differed widely in their antirachitic value for infants. Hess and Lewis stated that the ratios of human antirachitic potency of these substances in the order named was 15:8:1; in other words, 15 rat units of viosterol have the same antirachitic action in the infant as 8 rat units of yeast milk or 1 rat unit of directly irradiated milk. In a recent critical review of the literature on vitamin D milk, additional evidence has been collected concerning this variability in human antirachitic activity of fortified milks containing the same number of rat units of vitamin D.[3] Obviously, in the present state of our knowledge the only true evaluation of antirachitic potency for infants of a new vitamin D fortified milk must be actual clinical trial.

The evaporated milk employed in this investigation came from one pooled batch of milk to insure uniform composition. One portion of the evaporated milk was subjected to three seconds of irradiation by the carbon arc lamp, the evaporated milk flowing in a constant film over the interior of a cylinder in the center of which burned the carbon arc. Another portion of the same milk was canned without irradiation. Assays of the vitamin D content of the irradiated milk performed at the Children's Hospital of Philadelphia showed that there were approximately 125 U.S.P. units* of vitamin D in each 14.5 ounce can of milk. Since all the irradiated milk used came from one pooled batch, the constancy of vitamin D content from can to can was assured. Furthermore, assay of the milk at the beginning and end of the study indicated that there was no appreciable change in the vitamin D content

From the Children's Hospital.
The funds for these studies were furnished by the Wisconsin Alumni Research Foundation.
*Approximately equivalent to 45 Steenbock units.

during the four-month period covered by the investigation. The evaporated milk which was not subjected to ultraviolet irradiation was used for preliminary feeding as will be described. This nonirradiated milk showed approximately 30 U.S.P. units per can.

Twenty-four infants were selected for this study according to the following criteria:

1. Race

   The infants were all negroes. They were selected because of their greater susceptibility to rickets.

2. Age

   The infants were all under five months of age at the beginning of the study. Table I indicates the age distribution of the infants.

TABLE I

AGE IN WK.	NUMBER OF INFANTS
1- 4	1 (9 days old)
5- 8	10
9-12	4
13-16	4 (1 later withdrawn from study)
19-20	5

   The age limit was chosen because it was felt that infants in this age period were growing actively and were highly susceptible to rickets.

3. Sex

   Male infants only were chosen. Calcium and phosphorus balance studies were made on all infants in the series (the results of which will be reported later). Male babies were selected because of the greater ease in collection of urine.

4. Health

   A. Rickets

      As far as possible the attempt was made to select infants who were free from rickets. This was not entirely possible, and five had a mild degree of rickets at the beginning of the study.

   B. Tuberculosis

      Physical examinations and Mantoux tests showed freedom from tuberculosis.

   C. Syphilis

      Serologic studies and physical examinations showed that all the infants were nonsyphilitic.

The study was carried out during the winter and spring from Jan. 2, 1934, to May 15, 1934, thereby minimizing any slight antirachitic effect of the sunlight coming through the glass windows of the ward in which the infants were kept.

All of the infants were hospitalized during the entire period of the

study. We believe that more careful observation of the progress of the infants, more accurate records of actual intake of milk, and the better elimination of other factors which might exert an antirachitic effect are assured on the hospital ward than in the out-patient clinics. Furthermore, balance studies of calcium and phosphorus are obviously impossible with out-patients.

The infants were quartered in one ward in the Children's Hospital of Philadelphia. This ward was isolated from the rest of the hospital, and each infant was in a separate glass-inclosed cubicle. A complete history was taken and a physical examination performed on each infant before he was admitted to the ward. Complete blood counts, including examination for sickling of the red cells, were made on admission and before discharge from the ward. A daily record of each infant's weight was kept, and measurements of length, fontanels, and circumference of head, chest, and abdomen were taken at the beginning and end of the study. Roentgenograms were taken of an upper and lower extremity on admission and were repeated at approximately monthly intervals. At about the same intervals examinations were made independently by two of us (J. S. and M. R.) for clinical evidence of rickets, using as major criteria, craniotabes, beading of the ribs, and enlargement of the wrists. We adopted an arbitrary clinical scale for these signs, varying from one-plus to four-plus, in each instance; one-plus being a barely perceptible sign and four-plus a very marked one. In almost all instances blood was withdrawn for phosphorus and calcium determinations at approximately the same time that the periodic roentgenograms were taken. The latter were interpreted by Dr. Ralph S. Bromer, roentgenologist of the hospital. Consultations concerning the roentgenograms were later held with Dr. Edwards A. Park and Dr. Martha Eliot.

All of the infants were given nonirradiated milk for a period of about one month, at the end of which time they were divided into two groups, one remaining on nonirradiated milk and the other receiving irradiated milk. The initial control period served to eliminate the effect of any previous antirachitic therapy and provided as uniform a starting point as possible for the new antirachitic agent under consideration. This method of dividing the infants into two groups had a double purpose, namely, to test the preventive as well as the curative value of the irradiated milk.

The feeding program was uniform for each infant. The milk was diluted equally with water and 5 per cent of dark corn syrup was added. This mixture was offered to the infants at a level of 55 calories per pound of expected body weight. Tomato juice was given as an antiscorbutic agent at a level of 5 c.c. per pound of expected body weight. In addition iron, as ferric ammonium citrate, was fed, 1 per cent being added to the tomato juice. We were fully aware of the

fact that iron is usually without effect before the fifth month of life; nevertheless, because some of our infants had reached this age, it was considered best to add it to the dietary of all the infants. It is unlikely that the level of iron administered could have had any influence on the evolution of rickets, as it was far below the levels utilized by Brock and Diamond[4] in producing rickets in rats. Other than water, which was given ad libitum, nothing else was included in the dietary of the infants.

While the incidence of upper and lower respiratory tract infections seemed very large in these infants, the careful daily examinations may account in part for this. Any rise in temperature above 100° F. was usually accounted for by a mild upper respiratory tract infection. Many of these minor infections would certainly be overlooked in the homes from which these infants were taken. However, we do believe that there was a higher incidence of respiratory tract infection in the ward than there would have been in a similar group of infants in a well-baby out-patient clinic. This is in keeping with the experience of others concerning well infants in hospitals.

While the plan of our study differs in several respects from the procedure outlined by Eliot and Powers[5] for evaluating antirachitic agents clinically, we believe that the test to which we have subjected this milk is as rigid and severe as is possible. The infants were all actively growing negroes, receiving no other antirachitic agent than their milk. They were kept under the constant observation of trained observers. Furthermore, we believe that differences in environment and differences in handling which occur in studies on out-patients introduce variable factors which limit the value of the studies.

RESULTS

On the whole the clinical evidences of rickets were usually in agreement with the roentgenologic evidence. However, in some cases we found a lack of agreement (Table II). Since the clinical signs were recorded independently by two observers and were found to coincide, we believe that the subjective error in our clinical observations has been reduced to a minimum. While the value of enlargement of the costochondral junctions as evidence of rickets may be questioned, craniotabes has usually been accepted as a sign of rickets in the absence of any other known causes of craniotabes, e.g., syphilis. That this is not always true is apparent in Table II, in which are listed five infants who showed definite craniotabes which we are quite certain was not the physiologic craniotabes of infants, and yet there was no roentgenographic evidence of rickets. Jundell[6] in a study of the clinical significance of craniotabes concluded that it is not necessarily a rachitic phenomenon.

In Table II it will be seen that a clinical diagnosis of rickets in eleven of the twelve infants was made before roentgenographic evidence appeared. Since the consensus is that the roentgenogram is the most trustworthy criterion, in Tables III, IV, and V, the diagnosis of rickets rests entirely upon the roentgenographic evidence.

Table III summarizes the course of nine infants (B, D, E, G, J, K, L, Y, Z) who were free from rickets roentgenologically when they were placed upon the irradiated evaporated milk, after having been on the nonirradiated evaporated milk for periods of three to eight and one-half weeks. Seven of these infants continued to be free from rickets while two (E, Y) developed rickets which began to heal spontaneously while they were on the same irradiated milk. Clinical signs of rickets

TABLE II

LACK OF AGREEMENT BETWEEN CLINICAL AND ROENTGENOGRAPHIC EVIDENCES OF RICKETS

INFANT	TIME	CLINICAL SIGNS OF RICKETS			X-RAY EVIDENCE OF RICKETS	SUBSEQUENT COURSE OF INFANT
		CRANIOTABES	BEADING OF RIBS	ENLARGEMENT OF WRISTS		
A	1/ 2/34	0	Moderate	Slight	0	Developed rickets, shown by x-ray and increase in clinical signs.
D	3/13/34	0	Slight	Questionable	0	Beading increased moderately, but x-ray never showed rickets.
E	3/13/34	0	Slight	0	0	Developed rickets, evidenced by x-ray and increase in clinical signs.
F	1/ 6/34	0	Moderate	Slight	0	Developed rickets, evidenced by x-ray and increase in clinical signs.
J	4/ 7/34	Slight	Slight	Slight	0	X-ray never showed signs of rickets. Beading increased moderately.
K	3/13/34	0	0	Slight	0	X-ray never showed signs of rickets. Developed slight beading, which persisted.
Q	1/16/34	0	0	0	Mild rickets	Subsequently developed a mild beading while x-ray still showed rickets.
S	1/16/34	Slight	Moderate	Slight	0	Developed exaggeration of his clinical signs along with x-ray signs of rickets.
T	1/16/34	Moderate	Moderate	Slight	0	Developed exaggeration of his clinical signs along with x-ray signs of rickets.
U	3/ 2/34	Slight	Moderate	0	0	Developed exaggeration of his clinical signs along with x-ray signs of rickets.
Y	2/14/34	0	Slight	0	0	Developed rickets by x-ray and increase in clinical signs.
Z	4/ 7/34	Slight	Slight	0	0	Never developed x-ray signs of rickets; craniotabes persisted.

TABLE III

PREVENTIVE EFFECT OF IRRADIATED EVAPORATED MILK

INFANT	AGE AT START	WEIGHT AT START	RICKETS AT START	CONDITION AT END OF PERIOD ON NONIRRAD. EVAP. MILK	GAIN IN WEIGHT ON NONIRRAD. MILK EVAP.	PERIOD ON IRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON IRRAD. EVAP. MILK	GAIN IN LENGTH IN INCHES (4 MO.)	RESULT
B	15½ wk.	9 lb. 12 oz.	None	On milk 5 wk. No rickets.	3 lb. 3 oz.	On milk 12 wk. Took 12 oz. (103 units vit. D) daily.	2 lb. 1 oz.	1½	Never had rickets at any time.
D	4 wk.	9 lb. 1 oz.	None	On milk 6 wk. No rickets.	2 lb. 7 oz.	On milk 11 wk. Took 12¼ oz. (105 units vit. D) daily.	3 lb. 8 oz.	5	Never had rickets at any time.
E	7 wk.	9 lb.	None	On milk 6 wk. No rickets.	3 lb. 7 oz.	On milk 12 wk. Took 12 oz. (103 units vit. D) daily.	3 lb. 9 oz.	4¾	Developed a very mild rickets after 8 wk. on irrad. evap. milk. Healed after 4 wk. on same milk.
G	9 wk.	12 lb. 13 oz.	None	On milk 4½ wk. No rickets.	2 lb. 12 oz.	On milk 12 wk. Took 13½ oz. (117 units vit D) daily.	4 lb. 1 oz.	3½	Never had rickets at any time.
J	6 wk.	6 lb. 8 oz.	None	On milk 4½ wk. No rickets.	1 lb. 12 oz.	On milk 12 wk. Took 10 oz. (88 units vit. D) daily.	4 lb. 3 oz.	5	Never had rickets at any time.
L	11½ wk.	9 lb. 8 oz.	None	On milk 3 wk. No rickets.	1 lb. 4 oz.	On milk 13 wk. Took 11⅜ oz. (101 units vit. D) daily.	3 lb. 8 oz.	3¼	Never had rickets at any time.
Y	5 wk. (twin)	6 lb. 13 oz.	None	On milk 8 wk. No rickets.	1 lb. 6 oz.	On milk 7½ wk. Took 10⅜ oz. (92 units vit. D) daily.	2 lb. 1 oz.	3½	Developed a moderate rickets which began to heal spontaneously on the same milk.
K	9 days	5 lb. 6 oz.	None	On milk 8½ wk. No rickets.	2 lb. 6 oz.	On milk 6½ wk. Took 10½ oz. (90 units vit. D) daily.	2 lb. 4 oz.	4½	Never developed rickets at any time.
Z	8 wk.	8 lb. 8 oz.	None	On milk 7½ wk. No rickets.	3 lb. 9 oz.	On milk 4½ wk. Took 14¾ oz. (127 units vit. D) daily.	2 lb. 7 oz	5¾	Never developed rickets at any time.

were present in both infants in the absence of roentgenographic bone changes at the time they began taking irradiated milk. In these two infants who developed rickets, we have been unable to correlate this with any differences in rate of growth or level of vitamin D intake as reported by Wilson.[7]

Table IV shows the course of thirteen infants who had developed varying degrees of rickets while on nonirradiated evaporated milk and who were placed on the irradiated evaporated milk to test its curative value. Two infants showed almost complete healing. Three infants showed slight healing. In two infants there was an advance of the rachitic process before slight healing set in. In four infants there was no healing, and in two there was continued advance of the rickets. One of these two latter infants showed no healing after ten daily doses of 15 c.c. of cod liver oil. Again we were not able to correlate any change in the rachitic process in any of these infants with definite changes in growth or level of vitamin D intake.

One infant (C), whose course is summarized in Table V, did not develop rickets after a twelve-week period of consumption of nonirradiated milk. While it could be argued that this infant failed to gain much weight, we know that he was not malnourished at the end of this period but instead grew from a short stocky infant into a long slender one. Moreover, some of the infants developed rickets during a period when they grew very little; in fact, Infant N developed rickets over a period during which he lost weight.

One infant (W), because of repeated illnesses necessitating therapeutic procedure which confused any interpretations of his clinical data, has been omitted from consideration.

The blood calcium and phosphorus determinations will be considered in detail in a presentation of the calcium and phosphorus balance studies. They were in approximate agreement with the roentgenographic and the clinical findings.

It was of interest that the administration of iron, as mentioned, affected favorably the hemoglobin level and the red cell count in only two of the twenty-three infants. One infant (W), whom we have omitted from consideration as far as the rickets was concerned because of illness, showed an increase of 10 per cent in the hemoglobin level while the red cell count remained the same. One infant showed evidence of sickling of the red cells without the accompaniment of clinical symptoms, which corresponds to the usual incidence in the Negro race.

DISCUSSION

From the evidence presented in Table III, irradiated evaporated milk containing 125 U.S.P. units of vitamin D per 14.5 ounce can appeared to be an adequate agent for the prevention of rickets in infants.

TABLE IV

CURATIVE EFFECT OF IRRADIATED EVAPORATED MILK

INFANT	AGE AT START	WEIGHT ON ADMISSION	RICKETS ON ADMISSION	RICKETS AT END OF PERIOD OF NONIRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON NONIRRAD. EVAP. MILK	PERIOD ON IRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON IRRAD. EVAP. MILK	GAIN IN LENGTH IN INCHES (4 MO.)	RESULT
A	8 wk.	10 lb. 8 oz.	None	On milk 12 wk. Moderate rickets.	3 lb. 1 oz.	On milk 5½ wk. Took 13 oz. (112 units vit. D) daily.	1 lb. 9 oz.	3⅜	Rickets progressed while on irradiated evaporated milk.
F	20 wk.	17 lb.	None	On milk 8 wk. Mild rickets.	2 lb. 2 oz.	On milk 8 wk. Took 15 oz. (129 units vit. D) daily.	8 oz.	1	Good healing at end of time.
H	20 wk.	14 lb. 12 oz.	Mild rickets	On milk 4 wk. Moderate rickets.	1 lb. 6 oz.	On milk 11½ wk. Took 10½ oz. (90 units vit. D) daily.	Lost 2 oz.	3	Rickets advanced at first then began to heal.
M	8 wk.	9 lb. 1 oz.	Very mild rickets	On milk 7 wk. Marked rickets.	2 lb. 7 oz.	On milk 8½ wk. Took 13½ oz. (114 units vit. D) daily.	1 lb. 13 oz.	4	Rickets stationary—no healing. Cod liver oil —15 c.c. daily for 10 days had no effect.
N	18 wk.	16 lb. 11 oz.	None	On milk 7½ wk. Moderate rickets.	Lost 3 oz.	On milk 5 wk. Took 12½ oz. (108 units vit. D) daily.	1 lb. 4 oz.	2	Beginning healing at end of period.
O	9 wk.	13 lb. 8 oz.	None	On milk 8 wk. Mild rickets.	3 lb. 3 oz.	On milk 7 wk. Took 14½ oz. (125 units vit. D) daily.	2 lb. 11 oz.	3	Rickets stationary—no healing.
P	16½ wk.	11 lb. 6 oz.	Mild rickets	On milk 5 wk. Moderate rickets.	7 oz.	On milk 10 wk. Took 12½ oz. (108 units vit. D) daily.	2 lb. 11 oz.	3	Rickets completely healed.
Q	7 wk.	10 lb.	Very mild rickets	On milk 6½ wk. Mild rickets with tetany.	1 lb.	On milk 9 wk. Took 10½ oz. (90 units vit. D) daily.	1 lb. 10 oz.	1¼	Tetany controlled by milk. Slight healing of rickets.
R	13½ wk.	13 lb. 2 oz.	None	On milk 10 wk. Moderate rickets.	2 lb. 3 oz.	On milk 4½ wk. Took 10½ oz. (90 units vit D) daily.	Lost 10 oz.	2½	Rickets stationary—no healing.

TABLE IV—CONT'D

INFANT	AGE AT START	WEIGHT ON ADMISSION	RICKETS ON ADMISSION	RICKETS AT END OF PERIOD OF NONIRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON NONIRRAD. EVAP. MILK	PERIOD ON IRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON IRRAD. EVAP. MILK	GAIN IN LENGTH IN INCHES (4 MO.)	RESULT
S	9½ wk.	12 lb.	None	On milk 3 wk. Very mild rickets.	1 lb.	On milk 12 wk. Took 11½ oz. (99 units vit. D) daily.	2 lb. 2 oz.	1	Rickets advanced slightly then good healing set in.
T	14 wk.	8 lb. 7 oz.	None	On milk 7½ wk. Moderate rickets.	1 lb. 14 oz.	On milk 8 wk. Took 10½ oz. (90 units vit. D) daily.	1 lb. 3 oz.	2	Rickets advanced slightly.
U	4½ wk.	8 lb. 12 oz.	None	On milk 10 wk. Mild rickets.	3 lb. 5 oz.	On milk 5 wk. Took 11 oz. (94 units vit. D) daily.	11 oz.	3½	Beginning healing at end of time.
X	5 wk. (twin)	7 lb. 12 oz.	None	On milk 10 wk. Marked rickets.	2 lb. 10 oz.	On milk 5 wk. Took 10¾ oz. (92 units vit. D) daily.	1 lb. 2 oz	3½	Rickets stationary—no healing.

TABLE V

INFANT FREE FROM RICKETS AFTER TWELVE WEEKS ON NONIRRADIATED EVAPORATED MILK

INFANT	AGE	WEIGHT AT START	RICKETS AT START	PERIOD ON NONIRRAD. EVAP. MILK	GAIN IN WEIGHT ON NONIRRAD. EVAP. MILK	PERIOD ON IRRADIATED EVAPORATED MILK	GAIN IN WEIGHT ON IRRAD. EVAP. MILK	GAIN IN LENGTH IN INCHES (4 MO.)	RESULT
C	18½ wk.	13 lb 8 oz.	None	On milk 12 wk. No rickets.	1 lb.	On milk 4 wk. Took 10½ oz. (90 units vit. D) daily.	8 oz.	3¾	Never had rickets. Grew from small stocky infant to long slender one. Not malnourished.

It should also be noted that two of the infants in this group who showed no roentgenologic evidence of rickets at the time they were put on irradiated milk developed mild roentgenologic evidence of rickets after the change. These signs disappeared rapidly while they continued to receive the same irradiated milk.

While the results in these two infants might be considered as evidence for the curative rather than prophylactic value of the irradiated evaporated milk, they were included in the above group, because of the criteria used for the diagnosis of rickets, i.e., they were free from rickets by roentgenologic examination at the time of the change from nonirradiated to irradiated milk.

From the evidence presented in Table IV, irradiated evaporated milk containing 125 U.S.P. units of vitamin D per 14.5 ounce can appears to be unreliable for the cure of rickets in infants. Although there were two infants who showed complete healing, three infants slight healing, and two infants an advance in the rachitic process followed by slight healing; nevertheless, there were four infants who showed no healing, and two infants in whom the rachitic process actually advanced without healing. It is possible that the last two infants fall in that group which is refractory to antirachitic therapy since one of them gave no evidence of healing even after ten days of therapy with 15 c.c. of cod liver oil daily.

Our data do not warrant any conclusions concerning the relationship between the severity of the rachitic process, the rate of growth in length and weight, and the amount of antirachitic agent administered, as noted by Wilson.[7]

Also, from these studies no conclusions could be drawn as to the variation in antirachitic value for infants of different antirachitic agents containing an equivalent number of vitamin D units by rat assay. The interesting studies of Waddell[8] appear to throw some light on this question.

SUMMARY

A study is recorded of the antirachitic value of irradiated evaporated milk, containing 125 U.S.P. units of vitamin D per 14.5 ounce can, in twenty-three male negro infants. This milk appeared to be an adequate agent for the prevention of rickets in negro infants. It also appeared to be an unreliable agent for the cure of rickets in negro infants.

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OBSERVATIONS ON POSTURAL TREATMENT OF UPPER RESPIRATORY INFECTION

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UPPER respiratory infection forms a constant and important problem in general medical practice just as it does in otolaryngology. This is especially true because one must deal not only with local infection in the nose and sinuses, but also with complications in the ears, throat, chest, and gastrointestinal tract.

Both general and local measures are employed to combat such infection. In regard to general measures in treatment I need make no comment save that recent years have brought changes in ideas and methods due to better understanding of physiology in health and in disease. A basis of scientific facts must always replace tradition and empiricism.

Considerable advance, too, has been made in our understanding of the nose and sinuses. Here physiology is concerned with the ciliated mucosa that forms the lining and functioning structure of these cavities. Much has been learned of the reaction, or response of this mucosa to disease and also to the various substances so commonly used in the nose for the purpose of treatment.

Normal physiologic activity in the nose and sinuses, to the extent that it concerns us here, consists of constant ciliary sweeping plus the steady outpouring of sufficient serous and mucoid fluid to keep moist the surface in which the cilia beat and to humidify the inspired air. All ciliary sweeping within the sinus is toward the ostium; all nasal sweeping is toward the pharynx. The final destination of all ciliary drainage is the mouth of the esophagus, where it is swallowed.[1]

Ciliary flow is at the rate of one-half a centimeter per minute, requiring about five minutes to pass from the anterior to posterior parts of the nasal chambers. This constitutes the chief cleansing and defense mechanism of the upper respiratory tract normally, and probably in disease as well. Other defense factors are present, such as phagocytic cells in small number, which wander throughout the mucosa, and antibodies in varying strength. The secretions are very slightly antiseptic due to the presence of lysozyme.

At the onset of infection defense is concerned with keeping up the ciliary cleansing, pouring out additional mucus, and mobilizing phagocytes and antibodies. These processes are more or less disturbed and

Read before the Academy of Pediatrics, Region IV Meeting, Oct. 26, 1934.

impeded by the bacterial toxins, and there is an initial sharp decrease in the effectiveness of lysozyme.[2]

The earliest sweepings of toxins and bacteria down the pharynx and toward the esophagus are of course the most toxic due to temporary lack of antibodies. Hence the early sore throat, laryngitis, malaise, and other symptoms.

When early resolution fails to take place, the infection progresses with more local discomfort and more disturbance of function. Nasal congestion occurs, and there is outpouring of mucopus in reaction to bacterial invasion of the mucosa. Congestion, overload of secretions, and prolonged contact with toxins impair ciliary activity, and further interference comes from drying of purulent films. Large areas of cilia may become paralyzed, allowing accumulations of mucopus. Sinus drainage is further impaired because blockage of the meatus cuts off the essential stimulation to ciliary activity that comes from the plus and minus alternation of air pressure during respiration.[3] Perhaps the worst interference is from drying, which paralyzes all affected cilia.[4]

Local treatment during a nasal infection can be of direct aid to some functions of the mucosa and of indirect aid to others. To be logical and effective it must tend toward removal of factors interrupting ciliary and other mucosal activities.

Shrinkage of the mucosa relieves congestion and restores the action from alternating air pressure. This alone goes far toward restoration of function. Emptying the nasal chambers of retained secretions and moistening the epithelium give further aid, as does also any actual stimulation of ciliary function.

How to accomplish these things with the least trauma, physical and chemical, is the essential problem. For it is obvious that to whatever extent a drug or method is harmful it counteracts whatever good it does.

Local measures commonly employed in treatment constitute a wide variety. Some physicians use tampons of silver protein; others employ drops of various substances, usually oily, applied with the head tilted back; others depend on sprays, or irrigations, or antrum washings, or simply throat swabbings with argyrol or mercurochrome. These procedures were devised at a time when nasal physiology was not so well understood as it is today.

Concerning the various drugs commonly used for treatment of the nose, recent experimental work by Lierle and Moore[5] and Proetz[6] is of prime interest. By using fresh ciliated epithelium from the human nose, the effect of drugs was studied at close range. These investigations although independently made were in striking agreement.

Physiologic salt solution appears to have no effect on ciliated membrane either for better or for worse. Tissue immersed in it for two

hours still functions. This is explained by similarity to the normal fluids of the nose.

Ephedrine, 0.5 to 3 per cent, in normal salt solution is also harmless. One investigator reported even sustained acceleration of ciliary activity in eleven of twenty tests.

With all other drugs and fluids used, we read a different story. Tap and distilled water and concentrated salt water are decidedly harmful as they quickly stop all ciliary activity. Mild silver protein (argyrol, neosilvol) causes definite slowing of ciliary activity. The slowing is explained as due to plain water solvent, which has to be used with these drugs, and also to precipitation or clumping of the drug over the surface. Cocaine in more than 2.5 per cent strength quickly causes slowing or paralysis of the cilia. Adrenalin, in a dilution of 1:1,000, causes immediate paralysis of the cilia, while a dilution of 1:5,000 causes slowing. Eucalyptol, menthol, thymol, zinc sulphate, and mercurochrome are all definitely harmful to ciliary activity. Merthiolate in dilutions up to 1:10,000 causes slowing of cilia. Mineral oil causes marked slowing of the ciliary stream, not so much by direct action on the cilia as from lying as a heavy inert blanket on the surface.

From all this we learn that ephedrine in normal salt solution stands out as the one preparation that we may use in the nose with apparently no harmful effect as regards physiologic function. It may even accelerate the ciliary beat. Also we know that ephedrine applied to mucous membrane contracts the capillaries and effectively reduces swelling and hyperemia, effects which are so desirable in infection.

It is apparent, furthermore, that most of the drugs commonly used in the nose do not produce the effect the physician intends. On the contrary they cause interference with vital defense processes, something he decidedly does not intend. For to slow or paralyze ciliary activity is to break down our most potent defense factor and to lend aid to the forces of infection. The recognition of nasal physiologic function no longer allows us to believe complacently that oil is harmless, or that colloids are soothing, or still less that mercurochrome in the throat cures infection that is in the nose.

Having, in ephedrine, an acceptable drug we need also a method of treatment based on the peculiar anatomy of the nose and sinuses. If we are open-minded, we must soon come to feel kindly disposed toward the use of the head-low posture. For only by posture can we hope to reach so irregular and intricate a labyrinth of spaces and structures.

Such use was recommended by Proetz,[7] of St. Louis, and the technic described by him has been in limited use for eight years. In the Proetz technic the patient lies on his back with his head hyperextended over the end of a table or cot to an inverted position. Treatment fluid is then instilled in the nostrils and gravitates to the superior nasal areas which are now dependent. It is thus intended to come in contact with and

bathe the upper meatuses and turbinates. Bear in mind that the sinus ostia are all in the upper half of the nose, and the sinuses are all involved to some extent in all colds.

However, there are several objections to the Proetz technic if considered as a possible routine procedure. First, it is designed to reach the sphenoid and posterior ethmoid area rather than to give equal distribution throughout the upper nose. This is inherent in this posture for it is difficult to get the patient's head sufficiently upside down. This causes the treatment fluid to miss the antrum and anterior ethmoid regions, which are very important. Second, this posture is often very uncomfortable, and, moreover, its strangeness tends to frighten children and to make them uncooperative. Third, on recovering from the Proetz position, the patient is usually unable to prevent the fluid nasal contents from pouring backward into the pharynx and mouth.

Nevertheless, it is believed that this concept marked a long step for-

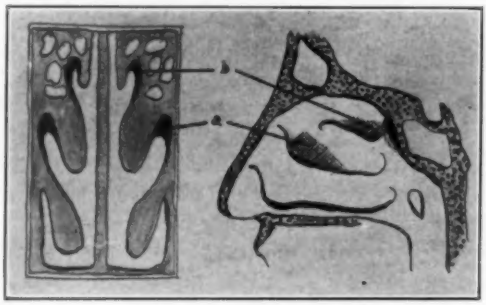

Fig. 1.—Schematic drawings of *A* cross-section of nasal cavity, and *B* lateral nasal wall. The sinus ostia are grouped in two areas as indicated; *a*, the anterior group (maxillary, frontal, and anterior ethmoid); *b*, the posterior group (sphenoid and posterior ethmoid).

ward in the direction of rational nasal therapy. It is fully realized that such things as posture and gravity normally are not factors in nasal and sinus drainage, but we are dealing here with congestion and purulent discharge, which are not normal findings and are often associated with marked abnormality of function as a result of disease.

A much simpler position for postural treatment has been found wherein the drawbacks mentioned are avoided. The desirable posture, of course, is with the head so inverted that the roof of the nasal chambers is at all times level or horizontal in the anteroposterior plane. Fluid instilled in the nose then would become equally distributed throughout the superior nasal areas and would bathe all regions where sinus ostia are found. To be practicable, the position must allow the patient to be sufficiently comfortable to retain the posture with ease for several minutes.

With the patient placed on his side and the lower shoulder somewhat elevated we can, by bending the head downward laterally, obtain a posture that approaches the ideal rather closely. A full description of this procedure was published a year and a half ago.[8]

With but little care this position is easily attained and can be held with relative comfort for as many minutes as desired. This is especially true of children because of their flexibility. As it is not too far removed from the side position in sleep, the element of fear is almost never present. A fact of prime importance is that while it is desirable to place the head in as nearly an upside-down position as possible, full inversion is not here essential. This is because in the side, or lateral, position the roof of the nasal fossae is at all times level in the anteroposterior plane, and is dependent just as soon as the head is bent below the horizontal.

The first step in treatment is to have the nose well opened by the use of an ephedrine spray or by topical application of ephedrine or

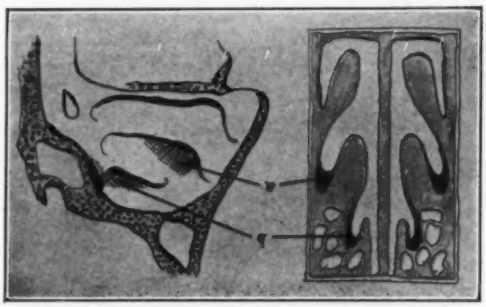

Fig. 2.—Same drawings inverted to illustrate the principle of posture in treatment. It will be seen how readily the upper meatuses and sinus ostia may be reached in this position by fluid instilled in the nose.

very dilute cocaine. Then with the patient in the lateral head-low posture the treatment fluid is instilled in the nostrils and flows by gravity to the now dependent superior nasal areas. For this purpose 1 per cent ephedrine in physiologic salt solution has been found satisfactory. The solution is first warmed to approximately body temperature.

The solution is left in for from three to five minutes. During this time the patient should breathe through the mouth. At termination of treatment the head is rotated to the position of face-down. This allows the fluid contents of the nose to run out of the nostrils and is assisted by gentle nose blowing. Since nasal contents need at no time enter the pharynx, there should be no annoyance from taste of the ephedrine, and none need be swallowed.

If, as part of the treatment, one wishes to have some of the ephedrine solution actually enter the sinuses, one may accomplish this by suction displacement.[9] From its known action ephedrine within a sinus will prolong the effect of treatment, and will favorably affect drainage by

reducing congestion and stimulating ciliary action. In acute conditions this has seemed unnecessary, but in cases in which the infection is subacute it has seemed distinctly useful, especially in children. In stubborn cases I have resorted to displacement many times with apparently favorable effect.

In practice the use of this method of postural treatment serves well as a routine procedure in the care of sinusitis and so-called bad colds.

Fig. 3.—Side view of child in lateral head-low position. More nearly complete inversion may easily be obtained as a rule but is not essential. This posture is reasonably comfortable.

Fig. 4.—End view of same posture. It is seen that the roof of the nasal fossae is approximately level in the anteroposterior plane; this is the essential thing as it insures equal distribution of the treatment fluid throughout the upper nasal areas.

This applies to both adults and children. It entails practically no discomfort. Since it does not traumatize the mucosa either physically or chemically, there is no local reaction. The procedure is easily carried out and requires no special equipment. It can be applied in any office and in any home. It can be repeated as often as desired. It requires a little more time and attention than is usually given these cases, but results fully justify this. Between treatments patients who are old enough can assist by the use of a spray of 1 per cent ephedrine.

Fig. 5.—Radiograph showing presence of lipiodol in all sinuses of both sides. Patient, an adult, was placed in the lateral head-low position and iodized oil instilled in both sides; this was followed by suction displacement. It illustrates the contact of the fluid used with all the sinus ostia.

Fig. 6.—Same as Fig. 5, lateral view.

Not only have results been good, but also certain desirable changes in the routine care of patients have been made possible. Thus the use of tampons and other similar procedures requiring intranasal instrumentation have been discarded. Postural treatment is more effective and at the same time is much cleaner and avoids all trauma to the ciliated mucosa. The common use of so-called nose drops, with home-use instructions to instill in the nose with the head tilted back has nothing to recommend it. Nothing could be more futile. Fluid thus used can do no more than run directly backward into the throat and can reach no higher than the dependent border of the lower turbinate. Ephedrine used in this way will produce only general symptoms from being swallowed, without local benefit. With the use of postural treatment, therapeutic antrum lavage is but rarely necessary. Postural treatment appears to give adequate drainage; it reaches both antrums at once; and it has the added advantage of reaching also the associated ethmoid cells that are so commonly involved with the antrum. Surgical antrum windows become necessary less often than formerly. One feels as if he has a means of greater control over these cases and hence can often avoid surgical procedures that would otherwise have seemed indicated.

It is frankly stated, however, that postural treatment has not been found of permanent beneficial effect in all long-standing cases. It does bring needed temporary relief from congestion and blockage. It does not supplant proper surgical intervention in cases in which permanent and constant relief is required, although this type of case appears to become less common. Its use in allergic nasal conditions is only palliative.

SUMMARY AND CONCLUSIONS

The most important physiologic activity of nasal and sinus mucosa, in regard to infection, is ciliary sweeping.

The purpose of all nasal treatment is to relieve the ciliated mucosa of a pathologic load of congestion and secretions and promote its ability to carry on more efficiently. Ephedrine in normal salt solution has been shown to be the drug of choice for this purpose; it is entirely harmless to ciliary activity, and it effectively reduces mucosal congestion and restores physiologic function.

The use of the lateral head-low posture is believed to be the rational method of applying treatment because it is based on anatomic and physiologic principles peculiar to the upper respiratory tract.

Those of us who have used this plan of treatment have obtained distinctly favorable results in the control of colds and acute and subacute sinusitis.

The prevention of undue progress in every cold is important, not only for present health, but also in the prevention of complications and chronic infection with their added difficulties.

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CONGENITAL RHABDOMYOMA OF THE HEART ASSOCIATED WITH ARRHYTHMIA

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IN 1931 Farber[1] contributed a very complete review of the known cases of cardiac rhabdomyoma, at that time totaling forty-one. He reemphasized the frequent association of this type of tumor with tuberous sclerosis of the brain and embryonal cysts of the kidney. Since his report two other cases of rhabdomyoma have appeared in the literature. Yater,[4] in a series of cardiac tumors, had one case of rhabdomyoma occurring in a colored child five years old who came into the hospital because of convulsions. The heart at necropsy contained two subendocardial nodules of tumor tissue, one of which was in the interventricular septum very close to, but not invading, the left bundle branch. The child also had tuberous sclerosis of the brain and renal cysts. Reitano and Nucciotti[3] presented the case of an infant who was intensely cyanotic and died in the first day of life; at necropsy was found an enormous tumor of the heart, which was thought to be a rhabdomyoma. It had multiple seats of origin, and the writers believed that it originated from the primordial undifferentiated cardiac cells. There were no abnormalities in any other organ.

It has been a matter for conjecture, as is mentioned by Farber, that in no instance has abnormal cardiac rhythm been part of the clinical picture of this condition, despite the fact that the tumor has usually been widespread. Indeed, many writers have supported the theory that the tumor arises from the Purkinje cells of the conduction system because of the similarity between the two types of cells. At present, however, the preferred theory is that the tumor arises from the primordial cells before they are differentiated.

The following case is reported because it seems to represent the first occasion that cardiac irregularity has been noted in this disease. The irregularity was the outstanding clinical finding and the reason for which the child was referred to the hospital.

M. A. M., a ten-month-old Italian female, was brought to the New Haven Hospital by her parents on Dec. 10, 1933, at 2:30 P.M., because of tachycardia which was discovered by her physician, Dr. W. C. McGuire, of New Haven.

The family history was not significant; the patient was the only child; and the parents were young, healthy individuals.

From the Departments of Pediatrics and Pathology, Yale University School of Medicine, and the Pediatric Service of the New Haven Hospital and Dispensary.

The birth and neonatal histories were negative. At the age of one month the child was seen in the well-baby clinic and was noted to be poorly nourished (weight 6 pounds 10 ounces). Subsequent visits were made only for minor feeding difficulties, but different observers felt that progress was not entirely satisfactory although no definite abnormalities were noted.

Except for colds there were no illnesses until at the age of seven months when the patient suddenly had a convulsion lasting ten minutes and consisting of stiffening and cyanosis. A physician who was called found no obvious cause for this. At the next visit to the clinic the fontanel was found to be closed, and the head was thought to be small. The baby was very fidgety, and the note in the record at this time contained a warning to "watch for neurologic phenomena."

Nothing untoward happened for the next month, but the mother then became afraid that the child was developing rickets and took her to a physician who increased the cod liver oil from two to six teaspoons daily. During the following month, that preceding admission, the parents observed that the baby experienced sudden transitory periods of pallor.

Two days before admission the patient seemed ill, was irritable, and vomited several times. The physician was called again and, as physical examination was negative, thought the vomiting might be due to an excess of cod liver oil and ordered the latter reduced. The next day the baby seemed better, but the pallor was observed again.

At 2:00 A.M. on the day of admission the mother was awakened by a cry from the child's room and found her extremely pale and "looking as though she were going to have a convulsion." She improved after a warm bath and an enema and slept through the night. After her morning milk she vomited and again became pale, remaining so until the physician was called at noon. Examination disclosed a very rapid heart rate, in addition to the pallor, which was marked, and she was referred to the New Haven Hospital.

On admission the temperature was 37.9° C., and respirations, 25 per minute. The color was good, neither pallor nor cyanosis being present. (The parents commented on the change from a half hour previously.) Positive findings were limited to the heart which was not enlarged to percussion. The sounds were of tictac quality, and the rate too rapid to be counted, estimates ranging from 220 to 300. The rhythm was irregular and consisted, according to one observer, of rapid regular beats in periods of varying length, interspersed with short periods of apparently complete stoppage. Another observer thought the intervening periods were not due to cessation but rather to slowing of the beats. The periods of rapid regular rhythm varied from a few seconds to several minutes. Pressure on the carotid sheaths produced slowing and greater irregularity, but release was followed by prompt return to the former state.

Laboratory Data.—R.B.C., 5.0; hemoglobin, 97 per cent (Sahli); W.B.C., 20,000; polymorphonuclear leucocytes, 58 per cent; lymphocytes, 40 per cent; monocytes, 2 per cent; smear, negative. Urine: albumin, one-plus; acetone, two-plus. Body weight, 7,950 gm. Head circumference: occipitofrontal, 42 cm. (average for this age is 43 to 44 cm.). Chest circumference, 42 cm. Length, 71 cm.

Fluoroscopy Report.—There was rapid, shallow pulsation of both auricles with a regular rhythm. Ventricular pulsations were shallow with a markedly irregular rhythm. There was no constancy in the time relation of the irregularity. Sudden diminution in the rapid beating of the auricular chambers followed compression of the carotid sheath.

Teleroentgenogram.—The heart shadow is within normal limits. The lung fields show slightly increased markings.

Electrocardiogram.—(Five hours after admission): (Fig. 1.) The rhythm is regular and the rate, 240. The configuration is consistent with a diagnosis of either tachycardia or auricular flutter with 1:1 rhythm. In view of the reaction to vagus pressure the latter is more likely. Unfortunately no periods of irregularity are included in the tracing.

It was decided to digitalize the patient, and one-quarter of her calculated dose (40 mg. per kilogram), 80 mg., was given subcutaneously at 8:00 P.M in the form of digifoline. No change was observed for the next three hours and at 11:00 P.M. she received another 80 mg. Almost immediately thereafter the heart was found to have slowed up and to have become more irregular. Her color and general appearance were still good, and in about five minutes the rate picked up again. A half hour later a nurse who was in the room saw the child turn blue suddenly and start to gasp. The interne arrived within the minute and was unable to detect any

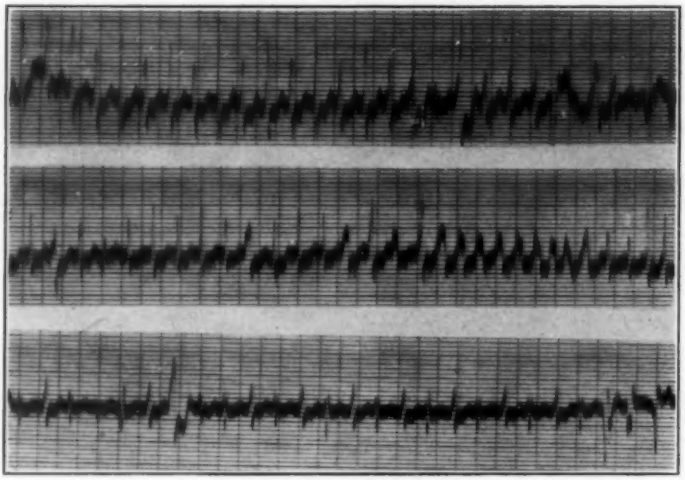

Fig. 1.—Electrocardiogram.

heartbeat although gasping respirations continued for another minute or two. Caffeine and adrenalin, the latter intracardially, failed to have any effect.

The clinical diagnosis was auricular flutter, presumably on the basis of some congenital anomaly.

NECROPSY FINDINGS

The body was very well developed and well nourished. There was no subcutaneous edema. The lips were slightly cyanotic. There were 75 c.c. of blood-tinged fluid in the right pleural cavity and 40 c.c. of a similar fluid in the left pleural cavity.

The findings of interest were confined to the heart and kidneys.

Heart.—The heart weighed 81 gm. The epicardium was intact, smooth, and glistening. The subepicardial fat was scanty. Externally, the red brown myocardium was a mottled yellow in many zones, especially along the course of the coronary vessels. The tricuspid valve had a row of small (1 to 3 mm. in diameter), raised, light yellow, fairly firm nodules along its line of insertion (Fig. 2). The endocardial surfaces of the right ventricle were smooth and glistening, but the mus-

culature of the columnae carneae and papillary muscles had a light yellow, mottled appearance similar to that observed on the external surfaces, only more marked and more extensive. This was most noticeable in the musculature of the interventricular septum. At the base of the papillary muscle of the medial cusp of the tricuspid valve, there was a nodular thickening 2 cm. in diameter which extended in to involve the interventricular septum. The anterior cusp of the mitral valve had a large, round, smooth nodule 2 cm. in diameter located at the point of insertion

Fig. 2.—Congenital rhabdomyoma of the heart. Nodules on (*A*) mitral and (*B*) tricuspid valves.

(Fig. 2). Its external and cut surfaces were light pink yellow and moderately firm. There were four smaller nodules from 2 to 5 mm. in diameter on the valve cusp. The endocardial surfaces of the left ventricle had a mottled light yellow color similar to the right ventricle. The mottled yellow color extended about halfway through the ventricle from the endocardial surface. The columnae carneae of both ventricles were rounded and their interspaces were deep and close together. The pulmonary and aortic valve leaflets were thin, delicate, and not unusual.

Microscopic examination of the heart showed the mottled yellow tissue observed in the gross in the myocardium of both the right and left ventricles to be represented by a neoplasm. There was a rather thin layer of tumor tissue just beneath

the epicardium. Most of the growth lay in the inner portions of the myocardium, a considerable amount being present in the papillary muscles. It invaded the myocardium diffusely and had very irregular and poorly demarcated borders. The nodules on the tricuspid and mitral valves consisted entirely of the same tumor.

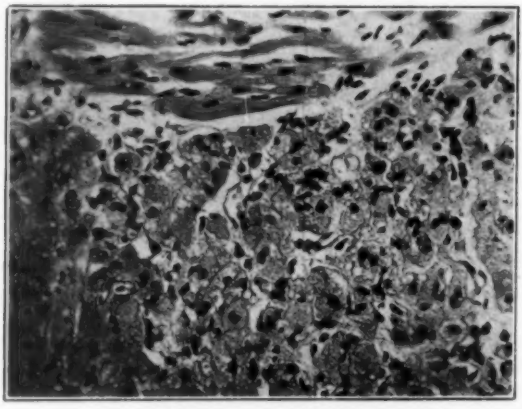

Fig. 3.—Tumor cells (below) with adjacent normal myocardium (above).

Fig. 4.—Site of conduction bundle; *M*, mitral valve; *T*, tricuspid valve; *A. V.*, auricular ventricular septum; *B*, blood vessels at site of conduction bundle; *R*, tumor nodule.

The tumor cells had a rather close resemblance to myocardial cells in their general appearance (Fig. 3); however, they were somewhat larger and stained light purple in distinction to the light red of the myocardium. Their arrangement was disorderly. They were more or less polygonal in outline and did not tend to be elongated like

myocardial cells, varying considerably in size and shape. Mitotic figures were not seen. The cytoplasm of the tumor cells was finely vacuolated. This vacuolization was fairly marked in some cells so that the cytoplasm appeared in rather fine, radiating strands, giving the appearance described in the literature as characteristic of rhabdomyoma.[1] This vacuolization was apparently not as marked in the cells of this case as in those of the case described by Farber. The nuclei of the tumor cells tended to be large. There was about as much stroma associated with the tumor tissue as with the normal myocardium. The architecture of the myocardium was quite distorted by zones of tumor tissue but was otherwise not especially unusual. Microscopic preparations of the myocardium were stained with phosphotungstic acid and with hematoxylin-eosin and by the Mallory aniline blue and the van Gieson methods. Striations were not distinguished in the rhabdomyoma cells.

Serial sections were prepared of the conduction bundle. Each preparation contained interauricular and interventricular septums with parts of the tricuspid and mitral valves attached. The latter valve was partly replaced by a large tumor nodule, and tumor tissue almost completely replaced the myocardium in these preparations. The conduction bundle itself could not be identified, but its site in the auriculoventricular connective tissue septum was distinguished by the fact that several arterioles and venules were seen to pass through the septum and to come to lie on the side of the right ventricle (Fig. 4). This region, which represented the site of the conduction bundle, was completely invaded by tumor.

Kidneys.—The kidneys contained numerous small cysts which were from 2 to 3 mm. in diameter and were filled with clear fluid. These cysts were scattered through the cortex and were best seen on the external surfaces. On microscopic examination they were seen to have a thick wall of connective tissue which was lined in most instances by a well-preserved, single layer of flattened epithelial cells.

Brain.—The cerebral findings were confined to minor architectural malformations in the cellular structures of the basal ganglions and the cerebellar cortex. There was no evidence of tuberous sclerosis.

Lungs.—There were numerous extravasations of blood beneath the pleura and into the pulmonary tissue.

DISCUSSION

Classification of the type of arrhythmia which occurred in this case is not easy. The irregularity observed clinically, coupled with the electrocardiographic tracing, would indicate auricular flutter with varying degrees of block as the most likely diagnosis. The episodes of pallor noted before admission might easily have been due to transient complete heart-block.

Cases of disturbance of the heart rate in young children are not rare and similar difficulty has been experienced in identifying the arrhythmia.[2] Various etiologic conditions for such disturbances have been recognized and probably the most frequent cause has been congenital heart disease. It would appear from this case that tumor of the heart must also be considered in the differential diagnosis of abnormal rhythm in infants.

The clinical aspects of many of the cases of rhabdomyoma have been confined to the cerebral symptoms associated with the accompanying tuberous sclerosis. Cardiac findings, when present, have been those of congestive failure. In the present instance the tumor was found

not only invading the cardiac musculature but completely obliterating the auriculoventricular bundle. This is apparently the first time that invasion of the conduction system has been demonstrated. It seems more surprising that there was so little cardiac difficulty rather than that there was any.

Whether the digitalis had any effect on the early death of the patient is problematical. The extensive involvement of the heart at necropsy and the fact that signs of cardiac disorder had appeared so recently and seemed to be increasing in severity would imply that the disease ran its natural course. However, while the dosage of the drug was far below the usual toxic range, the amount given, in a heart so seriously damaged, might have caused it to stop beating.

SUMMARY

A case of rhabdomyoma of the heart in a ten-month-old girl is reported. The most important clinical finding was a cardiac arrhythmia thought to be auricular flutter. At necropsy the tumor was found to invade the conduction system. Congenital cysts of the kidneys were also present.

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A STUDY OF THE SEASONAL INCIDENCE IN THE MORBIDITY AND MORTALITY OF TWENTY THOUSAND BREAST AND ARTIFICIALLY FED INFANTS FOR THE FIRST NINE MONTHS OF LIFE

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THE present paper is concerned with the seasonal incidence of disease among the same group of children referred to in an earlier communication.[1] Since these statistics covered a period of five years, it is not likely that the seasonal incidence of disease is to be much affected by differences in the type of infection which may occur, especially respiratory infection.

In the study of morbidity, any note on the chart that indicated any feeding disturbance, cold or respiratory infection, or other infection is classified as an infection. These were divided into three main groups: respiratory infections, gastrointestinal and unclassified.

In Tables I and II and Charts 1, 2, 3, 4, 5, and 6 the months are given seasonally as follows: March, April, and May, as spring; June,

TABLE I

SEASONAL MORBIDITY

		SPRING MAR. APR. MAY	SUMMER JUNE, JULY, AUG.	FALL SEPT. OCT. NOV.	WINTER DEC. JAN. FEB.
Breast Fed					
Respiratory	No.	799	311	698	929
	Per cent	8.1 %	3.2 %	7.2 %	9.5 %
Gastrointestinal	No.	70	193	171	70
	Per cent	0.72%	1.99%	1.76%	0.72%
Unclassified	No.	77	100	77	68
	Per cent	0.79%	1.1 %	0.79%	0.70%
Partially Breast Fed					
Respiratory	No.	877	410	614	1024
	Per cent	10.2 %	4.7 %	7.1 %	11.7 %
Gastrointestinal	No.	165	517	265	154
	Per cent	1.9 %	5.9 %	3.09%	1.79%
Unclassified	No.	150	113	83	170
	Per cent	1.75%	1.31%	0.96%	1.98%
Artificially Fed					
Respiratory	No.	240	146	93	186
	Per cent	14.1 %	8.6 %	5.5 %	10.9 %
Gastrointestinal	No.	35	129	74	35
	Per cent	2.29%	7.59%	4.35%	2.29%
Unclassified	No.	28	34	39	36
	Per cent	1.65%	2.0 %	2.29%	2.17%

July, and August, as summer; September, October, and November, as autumn; and December, January, and February, as winter. The

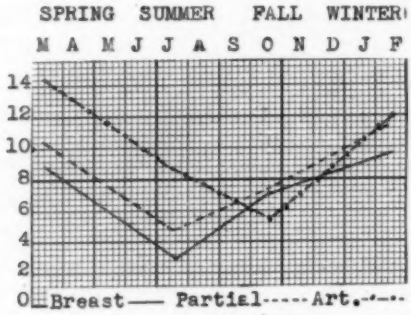

Chart 1.—Seasonal morbidity from respiratory infections.

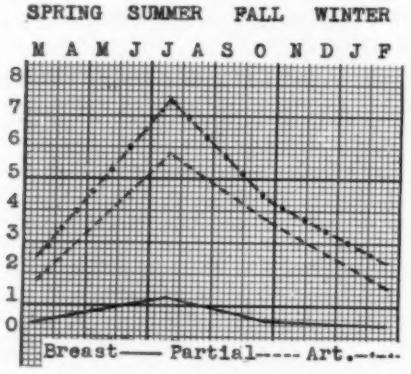

Chart 2.—Seasonal morbidity from gastrointestinal infections.

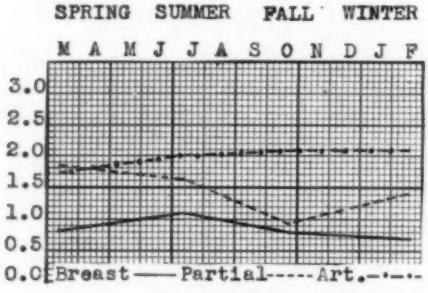

Chart 3.—Seasonal morbidity from unclassified infections.

exact number of cases is recorded for each season. Below this is given the percentage of these cases to the total number of infants in that group.

These percentages are also expressed graphically. In the charts, however, the statistics are recorded on a monthly rather than a seasonal basis.

As reported in the previous paper, there were 218 deaths during the five-year period, giving a total mortality of 1.1 per cent, or eleven deaths per thousand.

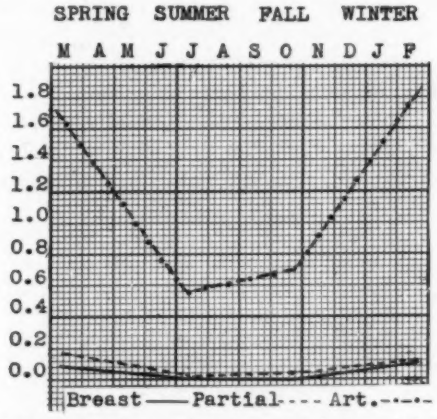

Chart 4.—Seasonal mortality from respiratory infections.

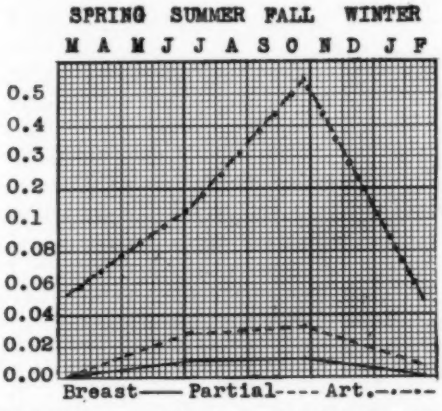

Chart 5.—Seasonal mortality from gastrointestinal infections.

Table II and Charts 4, 5, and 6 give the exact number of deaths by seasons with a percentage of total deaths (218) as in the morbidity. These percentages are also expressed graphically (by months).

DISCUSSION

The greatly increased morbidity and mortality of the artificially fed infant over the breast-fed and partially breast-fed child have been

discussed elsewhere and will not be repeated here. In all groups the respiratory infections are greatest in the spring, smallest during the summer, and increased during the fall and winter almost to the spring peak.

In gastrointestinal disturbances the curve for seasonal morbidity for the breast-fed baby is so low as to make it hard to record. There is a slightly higher incidence in the summer. Both the artificially and partially breast-fed groups show a low incidence in the spring, rising to an extreme peak in the summer and dropping through the fall and winter. Note that the total incidence of morbidity is twice as great in the respiratory disturbances as in the gastrointestinal.

In the unclassified infections the morbidity in the breast-fed group is low in the spring, fall, and winter, with a slight increase in the

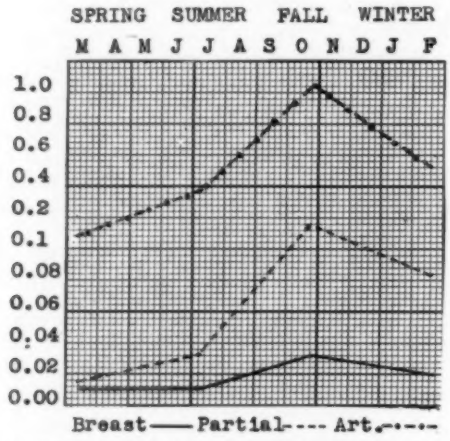

Chart 6.—Seasonal mortality from unclassified infections.

summer. The partially breast-fed group shows an increase in the spring and winter, while the morbidity of the artificially fed group is low in the spring and higher in the summer, fall, and winter.

We may say, therefore, in general, that in all types of feeding the morbidity for respiratory infections is greatest in the spring, lowest in the summer, and increases through the fall and winter to the spring peak. The gastrointestinal disturbances are low in the winter and spring and reach an extreme peak in the summer, decreasing through the fall. The unclassified infections are lowest in the spring.

In the seasonal mortality the curves follow in general those for morbidity, except for gastrointestinal disturbances. For these the greatest mortality is in the early fall, or October, when the morbidity curve is falling. Note the greatly increased mortality of the artificially fed baby in all seasons. Also note that the respiratory infection mor-

tality is about three times that of the gastrointestinal infections. The mortality curve in the unclassified infections rises more abruptly in the winter than does the morbidity curve.

TABLE II

SEASONAL MORTALITY

		SPRING MAR. APR. MAY	SUMMER JUNE, JULY, AUG.	FALL SEPT. OCT. NOV.	WINTER DEC. JAN. FEB.
Breast Fed					
Respiratory	No.	1			3
	Per cent	0.01 %			0.03 %
Gastrointestinal	No.		1	1	
	Per cent		0.01 %	0.01 %	
Unclassified	No.	1	1	3	2
	Per cent	0.01 %	0.01 %	0.03 %	0.02 %
Partially Breast Fed					
Respiratory	No.	15	5	7	17
	Per cent	0.19 %	0.061%	0.085%	0.021%
Gastrointestinal	No.		2	3	1
	Per cent		0.025%	0.037%	0.014%
Unclassified	No.	1	3	14	7
	Per cent	0.014%	0.037%	0.175%	0.084%
Artificially Fed					
Respiratory	No.	30	10	11	31
	Per cent	1.76 %	0.59 %	0.64 %	1.82 %
Gastrointestinal	No.	1	3	9	1
	Per cent	0.05 %	0.175%	0.532%	0.05 %
Unclassified	No.	2	5	18	8
	Per cent	0.10 %	0.29 %	1.05 %	0.47 %

CONCLUSION

The seasonal incidence of morbidity and mortality in this group of infants does not differ materially from the generally accepted ideas. In general the seasonal curve is not affected in its contour by the type of feeding. The height of the curve, however, is continually lowest in all seasons in the breast-fed infant.

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Pediatric Clinics

THE CHILDREN'S HOSPITAL
[KING EDWARD VII MEMORIAL]

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History.—The latter half of the eighteenth century was a momentous period in the foreign and domestic politics of Great Britain. Abroad, the American War of Independence was precipitated by a foolish King and his advisors, whilst at home there occurred the so-called Industrial Revolution. The Birmingham Children's Hospital has an interesting connection with this revolution, a period which proved in the most literal sense of the word a golden age for all but the labouring classes. The acquisition of wealth was, however, not the sole pursuit of that age; there was also a veritable renaissance of learning which led to the foundation of many philosophical clubs of which the Lunar Society of Birmingham was one of the most famous. The members of this Society were, not unnaturally, labelled "lunatics," but its name was due to the fact that the meetings took place when the moon was at the full in order that the members, having dined at two o'clock in the afternoon, could reach home by the light of the moon and thus obtain protection from attacks by the footpads who, at that time, infested the town. The Society included amongst its members James Watt, the inventor of the steam engine; his partner, Matthew Boulton, who became famous as a maker of Sheffield plate; James Wedgewood, the founder of the great pottery firm of that name; Erasmus Darwin, grandfather of Charles Darwin; Joseph Priestley, the discoverer of oxygen; Francis Galton, the physicist; and William Withering, the greatest physician Birmingham has ever had. Withering not only introduced digitalis into medical practice, but he was also a great botanist and chemist; indeed, he it was who suggested to Priestley the line of research which led to the preparation of oxygen. So famous was Withering that when he lay a-dying, a London contemporary who visited him is accredited with the aphorism, "The flower of English medicine is indeed withering." A meeting of the Lunar Society I am sure produced not only a good dinner, but also a feast of intellect and a flow of wit almost beyond imagination. It is because of this amazing collection of members that I like to think we can claim some slight association with the Lunar Society in the fact that the Hospital was opened on January 1, 1862, in the house which had been the home of Francis Galton—a house which incidentally has only disappeared within recent years to make way for a cinema!

This little institution of ten beds, founded largely as the result of the efforts of Dr. T. P. Heslop, had as its expressed objects:

1. To treat the sick children of the poor.
2. To increase knowledge of disease and to provide for more efficient instruction of students.

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3. To diffuse among all classes knowledge of the management of infants and children during illness and to train women as children's nurses.

4. To treat diseases peculiar to children and not to deal with surgical conditions.

Except for a slight modification of the last, these objects have been always kept in view although the instruction of students has only been achieved within recent years. The work of this small hospital increased so much that in 1870 a larger building was taken, which provided accommodation for sixty-two beds, nearly one-half of these now being devoted to the surgical conditions of childhood. In this building the work was carried on with varying fortunes for nearly half a century although long before the end of that time it was obvious that the building was totally unsuited for the work, and it became quite clear that if paediatrics was ever to have any standing in Birmingham, a hospital worthy of the subject must be erected. Fortunately the members of the mananging committee were men and women of vision and faith. They conceived a plan of a hospital of 150 beds which, however, for a few years it seemed impossible to implement, but on the death of King Edward the Seventh in 1910 an appeal was made that a Children's Hospital should be built as a memorial to him. This appeal was successful, building operations being started in 1911 only to be delayed by the European War, and although patients were received in the new hospital in 1917 it was not until 1919 that it was formally opened by His Majesty the King and then only for 100 patients. Since that time the development of the hospital has been continuous; the number of beds was increased to 160 in 1927; in 1924 an out-patient department was opened; in 1929 the number of beds was increased to 248 and an isolation block built; in 1932 a new nurses' home was built; and plans are now prepared for a separate infants' block which it is hoped may be ready for occupation in 1938 and which will bring up the number of beds to over 300. It is not anticipated that the hospital on its present site will ever increase much beyond that number of beds.

Hospital Practice in the United Kingdom.—Before describing the hospital it may be interesting to indicate some differences which hospital practice in the United Kingdom, and in many but not all parts of the British Empire, presents from that in America and elsewhere. First, our children's hospitals have been planned on general hospitals and therefore when fully equipped contain most of the departments usually associated with a general hospital and also certain departments which are not found in a general hospital. Thus in the Birmingham Children's Hospital there are:

111 beds allotted to general medicine
61 beds allotted to general surgery
26 beds allotted to ear and throat
5 beds allotted to ophthalmology
3 beds allotted to dermatology
8 beds allotted to orthopaedics
20 beds allotted to private patients
14 beds allotted to infectious diseases

In addition there are large dental and orthoptic departments; speech clinics for stammerers and children with palatal defects; venereal disease clinic; radiological, light, massage, and remedial exercise departments; bacteriological, pathological, biochemical, and pharmaceutical laboratories.

Second, the members of the visiting medical staff, with one exception, are unsalaried, although during the first six years of their service they receive a small honorarium of £40 ($200) per year. The only full-time salaried visiting medical officer is the pathologist. Appointments to the visiting staff are made by the Board

of Management at an open election, certain fundamental qualifications being necessary before a candidate is eligible to compete for election. In the case of a physician this is Membership or Fellowship of one of the Royal Colleges of Physicians, and for a surgeon, Fellowship of one of the Royal Colleges of Surgeons. On first election the successful candidate works in the out-patient department, but when he reaches a certain degree of seniority and as those senior to him retire, either voluntarily or under an age limit, he obtains charge of beds. In our hospital everyone is given charge of four beds on election and this number gradually increases, but in other hospitals there is a sharp dividing line between the senior members of the staff, who have charge of beds, and the junior members, who have charge of out-patients. It thus follows that the available beds are split up between a large number of people and no one has a predominating number; for instance, we have four medical wards each containing from twenty-five to thirty beds divided amongst six physicians. Each of the three senior physicians has one ward and the fourth ward is split up between the three junior physicians. The Professor of Children's Diseases has the right to have beds in the hospital but almost certainly the holder of this office will always be chosen from one of the physicians already attached to the hospital. There is no whole-time Professor of Children's Diseases in Great Britain or Ireland and I know of only one children's hospital in which there is anything approaching the post of *chef de clinique* such as occurs in other parts of the world. The holder of the professorial chair is therefore dependent upon his colleagues for much of the material for teaching purposes, and such a state of affairs might conceivably lead to difficulties, but I am happy to say that the attitude of my colleagues is one of helpfulness and cooperation and no such difficulties have ever arisen.

Third, all the members of the visiting medical staff make their living by consulting practice. The type of practice, so common in the United States and Canada, in which a paediatrician takes charge of the child throughout its childhood is unknown in this country; indeed, the visiting staffs of the majority of the teaching hospitals are debarred from general practice. For these reasons, and considering the large size of the staff of a children's hospital, many paediatricians do not limit their practice to children but are also attached to general hospitals and do consulting practice in adult medicine. There are many arguments both for and against the procedure although this is not the time to discuss them, but it may be pointed out as a curious and unfair anomaly that some general hospitals both in London and the provinces do not allow the physician in charge of the children's department to do adult practice, yet place no restriction on the general physicians who are allowed to, and do see, sick children.

Visiting and Resident Staff.—The visiting medical staff consists of six physicians, six surgeons, two ear and throat surgeons, one orthopaedic surgeon, two ophthalmologists, three dental surgeons, one dermatologist, two radiologists, an anaesthetist, and a pathologist. There are also a group of part-time salaried visiting officers who are not debarred from general practice—in fact some do not press a medical qualification—these include three anaesthetists, one ophthalmologist, a speech defect instructor, one orthodontist. In addition there are whole-time salaried officers, none of whom has a medical qualification; amongst these are four biochemists, orthoptic instructors, masseuses. The resident staff is composed of a resident medical officer, a resident surgical officer, and a casualty surgeon, all of whom hold office from one to three years; an assistant resident medical officer who holds office for twelve months; two house physicians and three house surgeons who are elected every six months. The assistant medical officer and each of the house physicians and surgeons are attached definitely to one or more members of the visiting staff, and there is no rotation of service such as is often the case in America and Canada.

Undergraduate Teaching.—Every medical student has to attend the hospital for instruction in his final and penultimate years; he has to attend twenty-nine clinical lectures and demonstrations given by the professor and other members of the staff and in addition acts as clinical clerk in the wards for a period of two (shortly to be increased to three) months. The clinical clerks have to attend for the whole of every morning. There is no special examination in paediatrics, nor does it appear likely that one will materalise in the near future, and although a student may be asked questions in children's diseases in his examination, yet he may graduate without ever having his knowledge of paediatrics tested.

Hospital.—The hospital was planned with two objects in view: first, to obtain the maximum amount of sunshine and for this purpose the main ward and the isolation block are built somewhat in the shape of a sector of a circle, the two arms of which face southeast and northwest, respectively; second, to obtain the maximum amount of fresh air. A reference to the illustrations will show how the latter has been achieved. Each ward unit, of which there are eight, consists of one large ward which contains twenty-two beds arranged along one side only, the opposite wall being almost entirely composed of folding windows which when opened and folded back make the ward a completely open-air one. The small room (*A*, in the photographs) in the middle of this wall was originally intended for a room in which dressings could be carried out; actually it is now used for a warm room for children who require such an atmosphere. At the end of the main ward is a small room (*B*, in the photographs) which was originally intended as an observation ward for doubtful infectious cases but is now used as a bedroom for nursing mothers or sick nurses. Near the entrance of the ward are grouped the ward kitchen, linen room, room for examination of urine and stools, and the infant ward. The latter (*C*, in the photographs) contains eight cots, and this also is kept at a higher temperature than the main ward; and although there are many windows, all of which can be opened entirely, it is not possible to put the infants directly in the open air without taking them through the main ward.

In planning these wards we have made at least two errors. First, the accommodation for infants is insufficient and also inadequate in that it does not allow for proper isolation. In building our new infants' ward block, we are planning to have two infants in a cubicle and one nurse to each cubicle. Second, whilst it is possible to get children into the open air or even direct sunlight by wheeling their beds to the window side of the ward, it is only possible to put them completely outside on the ground floor; staggered balconies should have been provided for the other floors so that every child could be placed in the open air if necessary.

The isolation block, *H*, has the sisters' duty room in the middle; on one side of this are a row of five rooms, divided from the sisters' room and from each other by walls chiefly made of glass, so that the sister can see the whole length of the ward from her desk; on the other side the ward is not divided up. Running along the back of all these is a connecting corridor which in its turn connects with a sanitary annexe. Each of the little rooms contains running hot and cold water and a large window which opens so that the cot can be pushed outside. These rooms normally have one or two beds but will take three under pressure and are used to accommodate:

(a) Children who develop infectious diseases in the hospital and are too ill to be transferred to the city infectious hospital.

(b) Children who on admission to hospital are known "contacts" with infectious disease.

(c) Those with surgical conditions complicating infectious disease which cannot be adequately dealt with at the infectious hospital.

The large ward is used as a fallow ward to house contact children when an infection breaks out in a ward, or for the treatment of special epidemics with which the infectious hospital cannot deal adequately.

The wards on the one side and the nurses' home, *I*, on the other look out over a garden which in the spring and summer has all that charm and loveliness associated with an English garden and in which the children are allowed to play. Twenty years ago a large part of the garden was a slum promoting ill health in poor children; now its value as an educative and healing influence on the same type of children cannot possibly be overestimated.

One of the wards on the top floor is used as a private ward, and on this floor also the space which on the other floors is occupied by the infants' ward is used for surgical theatre accommodation. There are two theatres, one of which is specially equipped for ear, nose and throat surgery. The private ward differs little from the

Fig. 1.—Aerial view of the hospital building: *A*, warm room; *B*, bedroom for nursing mothers or sick nurses; *C*, infant ward; *D*, administration block; *E*, out-patient department; *F*, pathological block; *G*, laundry and boiler house; *H*, isolation block; *I*, nurses' home.

other wards except that the main ward is broken up into three smaller units by glass partitions. Scarcely any provision has been made for the child's mother or nurse to remain with him; indeed, unless the mother is nursing the baby, this practice is discouraged, but it is probable that in the future this accommodation may become necessary. The hospital charge for a private patient is £4. 14s. 6d. ($23.50) a week, medical fees being charged in addition. Sometimes patients who cannot afford these charges are admitted to this ward; under such conditions the hospital fee is reduced to £3. 3. 0 ($16.00) per week, and medical fees are also reduced. This figure leaves the hospital a small margin of profit since the cost per bed in the whole hospital works out at £2. 17s. 6d. ($14.50) per week; incidentally, during 1934, 3,500 patients were treated in the hospital, the average length of their stay being twenty-one days.

The kitchens, dining rooms for nursing and resident staffs, quarters for resident medical officers, bedrooms for some nurses and for maids, together with the ad-

ministrative offices, are in a block, *D*, which roughly runs parallel with the ward block. There is a central milk room in the ward block where all the feedings for infants are prepared. The hospital obtains tuberculin-tested milk from one herd of cows, but for greater security this is also pasteurised in the milk room. Every nurse during her training spends six weeks in this department so that she becomes familiar with the methods of milk preparation.

Connected with the main hospital block by a covered passage is a large out-patient hall, *E*, larger than is common in America. This department consists of a large central hall, grouped around which are consulting and examination rooms, almoners' and registration offices, operating theatre, isolation, plaster, and eye and ear and throat rooms. Adjoining the operating theatre is a ward of twelve beds in which children are housed for at least one night after operation for tonsils and adenoids. In the basement of this department is the pharmacy with its separate waiting hall; a buffet where parents and children can obtain refreshment at a small cost; biochemical

Fig. 2.—View of ward block showing folding windows: *A*, warm room; *B*, bedroom for nursing mothers or sick nurses; *C*, infant ward.

laboratories; workshops and storerooms. The size and work of the out-patient department may be gathered from the fact that the number of patients' attendances is over 100,000 a year and that in the same time 3,500 children pass through the small ward mentioned above.

The orthoptic department has a staff of four trainers and is a teaching school for orthoptic trainees. It deals with more than 150 children a year and is not only the largest but also was the first department of its kind in any children's hospital in the British Isles. Together with the orthodontic department it is at present located in some old dwelling houses in the hospital grounds which will later be replaced by new buildings.

The pathological laboratories, *F*, are housed in a separate building and the increase of research work and workers in recent years has rendered these and the biochemical laboratories inadequate for their purpose. Close to this block is the laundry, *G*, in which all the hospital washing is done and in which something like three-quarters of a million pieces are washed annually.

Nursing Staff.—The new nurses' home has accommodation for 120 nurses, all having single bedrooms, and in addition to recreation rooms there are classrooms, cookery school, and a lecture theatre equipped with epidiascope and cinematograph which is used for lectures to nurses and medical students. Nurses accepted for training must be over the age of eighteen years and must produce satisfactory evidence of general education. The number of nurses in training is ninety-nine; the course lasts three years, at the end of which those who adopt nursing as a profession usually proceed to an adult hospital for further three or four years' training. There are thirty-three graduate nurses distributed as follows:

Administrative Sisters	5
Ward and Department Sisters	14
Staff Nurses	14

None is allowed to hold the post of "sister" unless she is a registered "adult" nurse and has had experience in nursing children. The majority of "staff nurses," i.e., the post immediately below that of sister, are registered "adult" nurses, some of whom have had previous experience in children's nursing, whilst occasionally one of our own graduate nurses occupies the post.

Any description of the hospital would be incomplete without mentioning two affiliated institutions. First, about three miles away, set in a park of 20 acres, is a continuation hospital containing ninety beds to which children with tuberculous bones and joints and rheumatic heart disease may be sent for a prolonged period. The system of treatment for acute rheumatism includes a stay of three months or longer in the children's hospital, then for suitable cases a period of six months to two years at this continuation hospital and then a residential school. Second, the president of the hospital, Mr. C. Kunzle, a Birmingham citizen of Swiss nationality, owns a château at Davos, Switzerland, and during the last three years has received there over 100 children suffering from asthma, pulmonary fibrosis, emphysema, chronic cough, tuberculous peritonitis, tuberculous glands, etc., who have remained for varying periods of three months to two years. The children are under the care of Dr. Burckhardt of the Projuventute Kinder Sanatarium, and the hospital supplies one sister, one graduate nurse, one teacher and two nurses in training.

Research.—The hospital strives to live up to the object laid down by its founders "to increase the knowledge of disease in childhood" by stimulating research. The managing committee of the hospital spends on research what, for British hospitals, is a large sum of money, and in addition grants are made from the Medical Research Council and from the University Research Funds. A research scholarship of £400 ($2,000) per annum is awarded on my recommendation, the present holder (Dr. Carey Smallwood) is carrying out haematological research; facilities are also given for two other research workers to live and board in the hospital but without remuneration, and at the moment there is a vacancy for a rheumatism research scholar for a period of two years at a salary of £300 ($1,750) per annum. The senior biochemist (Dr. E. M. Hickmans) receives a personal grant from the Medical Research Council on the understanding that she spends half her time in research. In the past a considerable amount of research work has been done on bone dyscrasias in general, and on renal and coeliac rickets in particular, in the course of which much valuable help has been received from the radiological department (Dr. C. G. Teall and Dr. E. Thorpe); coeliac disease and infantile atrophy. Amongst the subjects which have occupied our attention now and in recent years are the anaemias of infancy and childhood; the anti-anaemic factors of yeast; the lipids in anaemia; the problems of tuberculosis of the childhood type; the spread of ward infections

amongst infants; the relation of vitamin A to coeliac disease; the control of scurvy by ascorbic acid and the value of qualitative tests of ascorbic acid in the urine as an index of latent scurvy; a comparison of the anti-rachitic effect of sunshine and skyshine in Birmingham with that in the open country; acute rheumatism.

The hospital is delighted to receive accredited workers from overseas, either as research workers or graduate students, and it may be a matter of interest to note that our pathologist, who came from the Babies Hospital, New York, on the recommendation of Dr. Rustin McIntosh and Dr. Alan Brown, and the resident medical officer who was sent to us from Rochester, N. Y., by Dr. S. W. Clausen, are Canadians and University of Toronto graduates.

I have now been on the staff of the Children's Hospital for twenty-four years and for a great part of that time have had a share in the development of its policy; therefore any attempt on my part to assess the hospital's progress and contributions to paediatrics, and to apportion praise for this, is a matter of considerable difficulty which I approach with diffidence. There is no doubt that in the pursuit of science, buildings and equipment are always secondary considerations and that it is men and women who count, yet in spite of that truism, buildings and equipment do play an important part. At any rate, prior to its move into its present quarters the Birmingham Children's Hospital was a parochial institution scarcely known outside Birmingham and regarded by the general hospitals of the city as a poor show which "cut no ice," and its staff had made but few contributions to paediatric research. After the War, however, a new era opened and the hospital began to take its proper place in the city, the reasons for this being:

(1) The vision of the managing committee and medical staff of a decade previously in planning and providing the nucleus of the present buildings.

(2) The appointment as superintendent of a young man of energy and vision who had been thoroughly trained in hospital management (Mr. H. F. Shrimpton) and who fortunately still remains with us to guide our policy.

(3) The realization by certain members of the medical staff that in spite of "the years that the locusts had eaten" on active service there were some problems worth attempting to solve in the difficult times of peace.

Some two or three years later two other appointments were made which greatly stimulated our work, namely that of our present nursing superintendent (Miss E. M. Cockeram) and a biochemist (Dr. E. M. Hickmans). In these early post war years also there sprang up a healthy friendly jealousy of Glasgow Children's Hospital, and during this time we believed that by our clinical work and investigations we were beginning to earn a reputation for the hospital. It was therefore a great blow to find that the hospital was not even mentioned in the list of British Children's Hospitals which appeared in Abt's *Paediatrics*. Chronologically the next most important factor in stimulating the development of the scientific side of the hospital was a visit I paid to the United States and Canada in 1925, in the course of which many valuable lessons were obtained and great inspiration received. On my way home I read with great interest Abraham Flexner's *Medical Education*, but his statement concerning Great Britain that "pediatrics with the exception already noted (Glasgow) does not in the modern sense exist" fanned the smouldering fire of jealousy of Glasgow into a flame of intense envy and anger. Although this statement seemed to me a trifle unfair, I registered a vow that I would try my best to stimulate my colleagues to wipe away the reproach. It is not for me to say whether we have succeeded, but the fact that the Editor has asked for this article and that we are delighted to receive many visitors from overseas makes me feel that we are beginning to breathe the same rarefied atmosphere in which our friends in Glasgow so deservedly

live! The last point which I would mention in the development of our clinic is the fact that in 1928 "in view of the importance of the research work carried on at the Children's Hospital" the University of Birmingham raised the status of the lecturer in diseases of childhood to that of professor, bringing the number of chairs in this subject in the British Isles to four (five since 1933).

Conclusion.—The Editor has asked me to describe something of the spirit of our hospital. To put into words and define the things of the spirit is always a difficult, nay, sometimes an impossible task, but to anyone who asks "can any good thing come out of Birmingham?" I would reply "come and see," for we should be delighted to demonstrate the spirit of the hospital. This spirit may, I believe, be expressed in four words: happiness, loyalty, enquiry, service—all of which are essentials if any children's hospital is adequately to fulfil its purpose. This hospital is a very happy place; we try by our actions to instil into the children that the hospital is a place in which to get and to keep well and that health and happiness go together. To this end the discipline is not rigid, all treatment and investigations being made as much a game as possible, and for this reason we do not hesitate to accept children for treatment in our speech defect and squint clinics who are otherwise in perfect health. The idea that attendance at a hospital makes a child fanciful and neurotic has been, in our view, completely exploded. Loyalty: the spirit of loyalty and helpfulness extends throughout all departments of the hospital, administrative, nursing, medical, engineering, etc.; everyone strives to make this hospital if possible the best hospital for children in this country. Enquiry: research is encouraged in every way, both in the wards and in the laboratories because we realize that without this stimulus the treatment of disease becomes stereotyped and eventually sterile; moreover, research is not limited to medical problems, and I might perhaps mention that recently it has included the best type of paint for wall surfaces and methods of cleansing and sterilizing babies' napkins. Finally, as with all who work for the sick, we have but one real object and that is to render the best service in our power to sick children and to give them the greatest chance to recover their health in the happiest possible surroundings.

Critical Review

PROGRESS OF PUBLIC HEALTH AS IT RELATES TO THE CHILD

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MORTALITY AND MORBIDITY

THE picture presented by mortality statistics in the United States for 1934 is somewhat less satisfactory than for 1933 or 1932, but rates were in general below those for 1931 and previous years. Preliminary figures made available by the United States Public Health Service[1] show a combined infant mortality rate of 58 for 1934 as compared with 56 for 1933, 57 for 1932, 61 for 1931, and 62 for 1930. Rates for diarrhea and enteritis in children under two years of age were slightly higher than in the preceding two years but still much lower than in 1931 or 1930. Deaths from pneumonia were increased over the two preceding years, but the rates for influenza and tuberculosis showed a marked decline. The rates for diphtheria, scarlet fever, typhoid fever, and poliomyelitis were all favorable. The two most striking increases were in the rates for measles and whooping cough, both of which rates were much higher than in any recent year. The actual rates for these diseases in the twenty-five states having 1934 figures available are shown in Table I for each of the past five years. These are population rates—age distributions are not yet available.

TABLE I

MORTALITY FROM CERTAIN CAUSES IN THE 25 STATES OF THE UNITED STATES WITH AVAILABLE DATA BY YEAR 1930-1934*

(Population July 1, 1934—80,813,000; Live Births, 1934—1,499,000)

DEATHS	1934	1933	1932	1931	1930
Per 1,000 Live Births					
Total infant mortality	58.0	56.0	57.0	61.0	62.0
Maternal mortality	5.4	5.6	5.9	6.2	6.2
Per 100,000 Population					
Diarrhea and enteritis (under 2 yr.)	11.1	10.0	10.3	14.0	17.8
Measles	4.2	1.6	1.5	2.5	2.9
Whooping cough	5.1	3.2	4.1	3.5	4.2
Scarlet fever	2.0	2.0	2.1	2.1	1.9
Diphtheria	2.7	2.9	3.8	4.1	4.6
Acute anterior poliomyelitis	0.6	0.6	0.7	1.9	1.1
Meningococcus meningitis	0.8	1.0	1.3	2.1	3.1
Influenza	15.2	23.7	27.5	24.8	18.5
Pneumonia, all forms	78.2	69.3	77.1	81.7	83.0
Tuberculosis, all forms	54.3	56.6	60.0	64.7	68.0

*Figures taken from Public Health Reports, U. S. Public Health Service, 50: No. 17, April 26, 1935. The states included are Alabama, California, Connecticut, District of Columbia, Georgia, Idaho, Indiana, Iowa, Kansas, Louisiana, Maryland, Michigan, Minnesota, Montana, Nebraska, New Jersey, New York, Ohio, Pennsylvania, Rhode Island, South Dakota, Tennessee, Virginia, West Virginia, and Wisconsin. (Mississippi, Illinois, and North Carolina are also included in some of the rates.)

Diphtheria death rates for the country as a whole have not declined as rapidly in the past four years as results in those states actively pressing for preschool child immunization have shown to be possible. This fact explains the selection of diphtheria prevention by the Committee of State and Provincial Health Authorities of North America as the subject for special emphasis in May Day health activities this year. Another incentive to renewed efforts toward securing a population immunized against this disease comes from the simplification of procedure incident to the perfection of alum-precipitated toxoid. The adoption of this agent as the one of choice for public health purposes seems to be generally favored at the present time. Its safety and effectiveness, used in a single injection of 1 c.c. (7.5 to 10.0 units) have apparently been adequately demonstrated.[2-6]

As to the incidence of reportable illnesses, measles and whooping cough were unusually prevalent throughout the country, accounting for the high specific death rates already referred to and probably also to a degree for the higher pneumonia rate. Poliomyelitis showed a high incidence in the Pacific and Mountain states, but the general picture throughout the country was not altered. Influenza remained generally inactive throughout the year, but 1935 opened with a mild wave of activity in progress. Scarlet fever also had not been prevalent but was generally on the increase at the beginning of 1935.

Exclusive of data on reportable diseases which, being communicable, tend to vary in incidence from year to year, and in contrast to the large mass of statistical data available on mortality rates, there have never been available any adequate data on the incidence of illness from different causes and among different age groups. Barring a few local studies such as those in Hagerstown, Md., very few investigations have been made of morbidity. Collins[7] has recently published extensive figures collected by the United States Public Health Service on the number and type of illnesses occurring within a given year among 9,000 families visited every two to four months, resident in 130 localities in eighteen different states and comprising 39,185 individuals. A comparison of the incidence of illness discovered in this way may be made with the mortality rates for corresponding states to give a rough picture of the expected fatality from different conditions at different ages. For example, at all ages collectively, respiratory diseases in this study represented the same proportion of all illnesses, as they represented of all deaths in the corresponding states, but they constituted a much higher proportion of illnesses than deaths at each age subdivision of childhood. It appears that illness rates are highest under five years and next between five and ten years of age, whereas death rates are higher after fifty-five years than under five and are extremely low between five and ten years. The fatality of illness is higher after fifty-five years than at any earlier age.* In the years before maturity, however, the general fatality of illness is highest under five years and lowest between five and ten years.

Such studies, if conducted at regular intervals, would give valuable information as to the changing prevalence and severity of different diseases, and offer a rough measure of the progress made in the prevention or modification of each.

*In this comparison deaths under one year are averaged into the first five. These statements would not apply if the first year were considered separately.

EFFECT OF DEPRESSION ON THE HEALTH AND GROWTH OF CHILDREN

Eliot reviewed the literature on this subject in this series of critical reviews last year.[8] Further evidence has been amassed during the year pointing to higher illness rates among the indigent than among the general population; and one such report[9] indicates that these rates are higher in those families made poor by the depression than in those previously accustomed to a low standard of living. It has always been possible to demonstrate higher illness rates, higher mortality, and poorer standards of growth among the low income classes than among the well-to-do; and as the proportion of the population in the lower income brackets increases, it is reasonable to assume that the health and growth of certain children are being adversely affected. A comparison of large groups including all classes today with similar groups during prosperous years, however, need not demonstrate these effects. The general trend toward better hygiene and nutrition operating with the majority of children may mask the adverse influences upon the children of the unemployed or poorly employed, who are still in the minority. Actually many investigators have been unable to demonstrate any mass evidence of retardation of growth among large groups of children after five years of continuing severe economic stringency. For example, Palmer[10] has made a comparison of annual weight gains of elementary school children in Hagerstown, Md., in two periods: the first, 1921-1927 and the second, 1933-1934. He found that the increments, while on the average definitely smaller for each grade in the latter period, were not smaller than occurred in single prosperous years. Here also the gains were strikingly smaller for the children of persons receiving aid than for those not so situated, but this difference was no wider than between similar groups in prosperous years. Newman[11] also reports similar findings in Great Britain; namely, that the depression has not measurably increased the amount of illness or malnutrition or the number of deaths among children—quoting from his report: ". . . the general health and nutrition of the population of England and Wales, taken as a whole, was well maintained in 1933 . . . there can be no question that the nutrition of the English people is better today than at any past period of which we have record. . . . This circumstance is due to the increased care and devotion of the mothers and teachers, to manifold forms of voluntary service, and to the public provision of insurance benefit, school feeding and medical supervision." We are, therefore, not warranted in being too complacent, but there is nevertheless justification for real satisfaction in the net results of community efforts to provide for the physical needs of children.

PUBLIC HEALTH SERVICES

In the first review in this series[12] it was pointed out that changes incident to the depression had not only interrupted progress in the development of state, municipal, and private services for the betterment of child health, but had actually caused serious interference with the activities of those already established in many parts of the country. In the second review[8] the changes incident to the depression were dealt with in more detail, and it was made evident that the facilities for meeting the health and medical needs of children in large sections of the country were far from adequate. Appropriations and expen-

ditures for child health activities in a majority of the states were shown to have experienced a further decline. In some states reductions in budgets or actual elimination of appropriations were shown to have seriously handicapped maternal and child health work. More recently[13] it has been shown that health departments in general maintained their appropriations through 1931, that some reductions occurred in 1932, but that the most drastic reductions occurred in 1933. This latter report estimated that the further cuts occurring in 1934 had reduced budgets to near the level of 1923.

It has become apparent to those seriously concerned with these changes that, although joint action by public health, medical and welfare groups can undoubtedly prevent further inroads into essential health services, financial limitations are bound to restrict the expansion of health activities for some time to come. A healthy emphasis has therefore become apparent upon the reexamination of programs, upon the demonstration of usefulness of procedures, and upon the selection of those of greatest value. Bishop[14] has summarized the outstanding trends in public health administration today and mentions among others the following: greater emphasis on the technical excellence of service and specificity of methods; increasing emphasis on special training of public health personnel; specificity of objectives and planning programs with subsequent analysis of results in view; and increasing appreciation of the fundamental importance of the state government in the public health program, with increasing interest on the part of the state health department in local health programs, especially in organization to meet rural health needs.

It has still more recently become apparent that the federal government is prepared to acknowledge its share of responsibility for securing at least a minimum of health service for mothers and children in all parts of the United States. The provisions of the "Social Security Bill" now before Congress are considered in more detail below. The point of interest in this connection is that federal appropriations for maternal and child health, for the crippled child, and for general public health services are made prominent and continuing features of this legislation.

RURAL PUBLIC HEALTH SERVICES

The "Social Security Bill" just referred to makes frequent and specific reference to the intent of Congress, through this legislation, to provide or strengthen public health services in rural communities, and all public health literature is filled with discussions of rural problems, especially those relating to the provision of adequate maternal and infant care. Rural communities have on the whole never received more than rudimentary public health services, and these largely from untrained personnel. Some of the progress that had been made in improving these conditions has recently been wiped out. During the year 1933 alone, health services with a full-time health officer in charge were discontinued in fifty-five rural units and were being newly established in only four.[15] As of Dec. 31, 1933, approximately fifteen millions out of the fifty-five millions comprising the rural population of the United States were served by such health officers. Even within full-time organizations child health services are very limited, and in communities without full-time health officers these activities are often

totally lacking.[16] In general, child health services are highly developed only in units in which the state, the United States Public Health Service or some foundation has aided in organization, administration, and finance.

PUBLIC HEALTH CONDITIONS IN FOREIGN COUNTRIES

While considering conditions in this country and before discussing pending legislation which if passed would materially alter conditions, it has seemed desirable to review briefly the major trends in certain foreign countries. There is such a wide variety of conditions present in different countries as to defy descriptive summary, but foreign experiments which have a bearing on our own problems may be brought to attention.

In the main the actual content of services and the procedures adopted have followed American lines, but they have been carried out in different ways and with varying emphasis. There has apparently been a greater tendency to combine social and health activities and a more predominant participation of government in medical services. As a result, the protection of the public health and the medical care of the sick have been less distinctly separated. Bolt[17] has recently sketched in outline present-day conditions and trends in certain European countries and has shown that the trend in Europe is decidedly in the direction of public control of the administration of all child health and welfare agencies. He finds an amazing interest in the health and well-being of mothers and children in all European countries and more ample provision for health services, despite desperate economic and governmental conditions.

In England "The Children and Young Persons Act of 1932" has further consolidated the regulations relating to the health of mothers, prospective mothers, and children, and under the "National Health Insurance Acts," prenatal and obstetric care and certain other maternity benefits are afforded all classes in the population. Through grants-in-aid the central government has done much to stimulate better local conditions. A recent project of far-reaching importance, which is given further consideration below, is that of extensive slum clearance and the construction by the government of low rental, small houses in the outskirts of cities. England has also made enviable progress in developing full-time public health units under specially trained health officers.

Bolt credits France with leadership in providing adequately for illegitimate children and their mothers and in provisions for the care of tuberculous children.

Germany appears to have been interested primarily in centralizing control of child health agencies already developed under local guidance, and regimenting them according to the dictates of national policy. This policy is fortunately directed toward the maintenance of the home and maternal care. Hence health services are organized for the family as a unit. Maternal and infant health centers are found in practically all the important cities of Germany. There are, for example, forty-six consultation centers for expectant mothers in Berlin alone.

In Italy the central government is furthering the development of health services through the National Institution for the Protection

of Motherhood and Infancy, but in general, emphasis on preventive medicine has lagged. It is hoped that the new Institute of Hygiene and Public Health in Rome will stimulate interest in this work. Italy has recently greatly extended the protection afforded working mothers through a decree[18] which provides for compulsory leave of absence from work before and after confinement, opportunity for nursing, insurance benefits, and investigation of maternal deaths.

Sweden's system of maternity benefits is an example of social insurance supplemented by national treasury contributions. Uninsured women with low incomes receive cash benefits for thirty days at the time of confinement, while insured industrial workers receive these for fifty-six days and in addition free midwife attendance, or hospital care if needed. Application must be made sixty days before the expected confinement, so that some prenatal care and plans for adequate delivery can be arranged. This system also allows for subsequent enrollment of the child in child health centers.

It is most difficult to appraise the value of health services from written reports. The plan may appear excellent on paper, but much depends upon the quality of work done, especially upon the training and ability of personnel, and one cannot make an estimate of these without close observation of work in progress. When political considerations dominate, the reporting evaluation is even more difficult. One even questions whether the reports of foreign visitors who acquire their information from hasty prearranged inspections or conversations with officials are really indicative of actual conditions. Reports from Soviet Russia relating to the progress of child health work bring all these questions vividly to mind. The observations of Newsholme, however, are of great interest.[19]

Child health activities in Soviet Russia have advanced from almost negligible levels to most extensive proportions under governmental auspices during recent years. This progress has been greatly facilitated by the virtual transfer of the care and control of children from parents to the state and the increased concentration of infants and children in public nurseries, schools and camps. It has gone hand in hand with welfare legislation affecting the economic and social status of women during pregnancy, the availability of medical care and the extent of health education. It has obviously been retarded by the dearth of adequately trained physicians and nurses. To show the rapidity of change, there were in the towns of R.S.F.S.R.* in 1932, 263,000 beds in crèches as against 34,000 five years previously, and there were in villages in the same year 329,000 permanent and 3,500,000 seasonal beds as against 2,500 permanent and 101,000 seasonal beds five years earlier. Crèches house infants from two months to three years, sometimes to five years of age, while their mothers work in industry. Health service is provided in connection with these, as well as in connection with kindergartens, which care for children from the ages of three to seven years, and schools and camps, which care for older children. Free attendance at infant consultation centers is also generally provided and is often made a condition of the mother's receiving maternity benefits. Newsholme states that the training, hygiene, and precautions against infection in the crèches are intelligent and "the quality of the provisions made for the hygienic and

*Russian Socialist Federated Soviet Republics.

medical care of infants bears comparison with any similar arrangements in western countries, and in quantity it is vastly greater."

There is in Russia no separation between clinical and preventive medicine because both institutional and domiciliary care have been socialized. There is reported to be close cooperation between home, medical attendance, and the health work in crèches and consultation centers.

Care of maternity in Soviet Russia is of special interest because of the attention which this subject deserves and is receiving in the United States. About 90 per cent of births in cities in Russia are now in institutions, new maternity hospitals having been provided on a liberal scale. Special consultation centers for pregnant women have also been established in all large cities. In rural areas, however, only about 20 per cent of deliveries are in institutions. Since the great majority of women in these areas are dependent upon midwives or relatives, the government has recognized the urgent need for more adequately trained midwives by providing a number of training centers. Insurance provides women in industry with extensive maternity benefits, including full wages during absence from work due to pregnancy and confinement, and money allowances during the nursing period. Infant mortality was reported for European Russia as 275 deaths per 1,000 live births in 1913, 186 in 1927, and 141 in 1930. The rate for Moscow was 130.9 and for Leningrad, 141.0 in 1929. The birth rate in these cities in the same year was 22 and 22.1 respectively; this despite the fact that in Moscow recorded abortions were 61 per cent in excess of normal births. Abortions were estimated to be ten times as numerous in 1929 as they were in 1922. Newsholme's description of medical education under the new regime and experience with regimentation of medical services elsewhere lead one to be somewhat skeptical as to the present quality of the various medical services described. One cannot doubt, however, that present conditions represent real progress.

There would seem to be little doubt that America has in recent years made more progress in the study of the child, especially of his health and medical needs, than has any other country. We undoubtedly have more physicians and other workers well equipped as specialists in the care of children. This review of activities in foreign countries raises the question as to whether we have as seriously faced the problem of making preventive health services, as well as medical services, available to all classes in all communities. With far fewer resources and greater handicaps as to adequacy of trained personnel, it would seem that other countries have been attempting to do more to assure a minimum of health protection to all. These considerations give point to the plans of our federal government for promoting maternal and child health and for general public health protection, as embodied in the present revision of the "Social Security Bill."

THE SOCIAL SECURITY BILL

The House of Representatives has recently passed the so-called "Social Security Bill" (H.R. 7260) and at the present writing this bill is awaiting consideration by the Senate Finance Committee. This is an omnibus bill providing the means for protection against a variety of social hazards, a number of which have indirect bearing on child health, but we are here concerned primarily with those provisions for

direct maternal and child health and public health services. Title V of this bill, "Grants to States for Maternal and Child Welfare," is divided into five parts. Part 1, "Maternal and Child Health Services," makes an annual appropriation of $3,800,000 for payments to states to carry out suitable plans for such services. Twenty thousand dollars is granted directly to each State and $1,800,000 apportioned on the basis of proportion of live births in each state. Only such portion of these allotments shall be paid to each state as does not exceed one-half of the total sum expended by the state exclusively for carrying out the accepted plans. An additional $980,000 may be allotted by the Secretary of Labor without regard to the amount of state contributions on the basis of financial need. This equalization fund takes into account the greater need of health services where resources are least adequate. Receipt of these sums is made dependent upon suitable administration, supervision, reports, cooperation with medical, nursing, and welfare groups, etc. Part 2 of Title V, "Services for Crippled Children," appropriates a sum of $2,850,000 annually to enable "each state to extend and improve (especially in rural areas and in areas suffering from severe economic distress) . . . services for locating crippled children, and for providing medical, surgical, corrective, and other services and care, . . ." This sum is to be allotted, $20,000 to each state and the remainder according to need, but in this case the amount paid shall not exceed one-half of the total sum expended. Part 3, "Child Welfare Services," appropriates $1,500,000 for cooperation with state public welfare agencies, $10,000 to each state and the balance on the basis of rural population. Part 4 increases the present grants for vocational rehabilitation, and Part 5 provides $425,000 "for all necessary expenses of the Children's Bureau in administering the provisions of this title." Oddly enough this provision for administration is made for one year only, whereas the title to be administered provides continuing services.

Title VI of the "Social Security Act," entitled "Public Health Work," appropriates $8,000,000 for "assisting states, counties, health districts, and other political subdivisions of the states in establishing and maintaining adequate public health services, including the training of personnel . . ." The primary purpose of this title is to secure for a far larger proportion of the counties a full-time public health organization, qualified to provide the essential services. The amount allotted in this case is determined by population, special health problems, and financial needs; matching with local funds is not required. An additional $2,000,000 is provided for expenditure by the Public Health Service for investigation of disease and problems of sanitation, etc.

Thus a total of about $17,000,000 is appropriated annually for health services, $7,000,000 under Title V for maternal and child health and care of crippled children to be administered by the Children's Bureau, and $10,000,000 under Title VI to be administered by the United States Public Health Service for general public health enterprises. Consideration is given in the bill to the uneven development of these services in different parts of the country, and especially to their general inadequacy in rural communities. It is also recognized that those communities least able to finance improvements are, in general, those most in need of strengthening their facilities. No consistent principle is

followed, however, as to the amount of local participation in carrying the costs of necessary services required under the different sections of the bill. It is provided that the bulk of the funds shall be spent locally under the direction of the states, with considerable latitude as to programs and services, but that certain standards shall be required by the federal agency.

The House of Delegates of the American Medical Association in special session went on record[20] as opposed to the administration of any health service by a lay bureau and specifically deplored and protested those sections of the "Social Security Act" (the original bill S. 1130) "... which place in the Children's Bureau of the Department of Labor the responsibility for the administration of funds for these purposes" (medical services for crippled children and for the preservation of child health and maternal health). However, at the Senate Finance Committee hearings on this original bill a large number of physicians, prominent in the field of pediatrics, recorded their approval of these health provisions. The organization of the federal government is such that the division of administrative responsibility between the two departments seems to be entirely logical and most certain to secure well-planned and supervised service. The assistant director of the Children's Bureau and the acting director of the Division of Maternal and Child Health are pediatricians with outstanding records of accomplishment and with the confidence of the profession. Title V will most certainly be administered by this Bureau in close cooperation with, and in many instances be applied through, the health units operated under Title VI by the Public Health Service.

Some may seriously question the desirability of the federal government's further participation in local services which the Social Security Act obviously provides, and many are concerned as to the economic implications of some of the other titles of this bill. The appropriations under Titles V and VI for health work are, however, relatively small. The health conditions in one section of the country are of vital concern to all others; and the problems in some sections are far more difficult than in others; a small equalization fund therefore seems warranted. Furthermore, the federal government can make available expert advice and general information which local communities are often not in a position to secure for themselves. There is every indication that both federal departments administering the health provisions under discussion will grant the widest local autonomy consistent with the maintenance of a high quality of work and a suitably trained and qualified personnel.*

HOUSING

Relatively little attention has been given in the past by public health authorities in this country to the effect of bad housing conditions upon child health, except so far as they concern water supply, sewage and garbage disposal, or adequate cubic feet of air space. It has been noted that in England health authorities have been placing great emphasis upon slum clearance and low-rent suburban residence building as a public health measure of importance. Other countries in Europe

*The act as at present written unfortunately witholds from the Children's Bureau any administrative control over the selection, tenure of office, and compensation of personnel secured under these grants (Title V, Sec. 503).

have been giving adequate housing considerable attention, and the accomplishments of Vienna are of special interest.[21] A new interest in this subject has recently been developing in this country, primarily as a result of the search for useful public works projects. Health officers have begun to realize the possibilities for improving public health through encouragement of slum clearance campaigns, and a number of studies on the relation of housing to health have appeared in public health journals.

It is not difficult to demonstrate a striking correlation between residence in slum areas[22] and abnormally high morbidity and mortality rates, but it is rather difficult to demonstrate that these relationships are due to the housing conditions per se, and not to regularly associated conditions such as race, ignorance, poverty, and overcrowding. Health authorities have not felt certain that without changing these other conditions, mere transference of families from dilapidated slum buildings to modern tenements would materially improve health conditions. Recent studies[23] do suggest, however, that the condition of the house itself and its immediate surroundings are of real importance and that the transference of families from condemned buildings to modern low-cost structures results in an immediate and definite improvement in mortality and morbidity rates. There are of course accompanying changes in living conditions which are inevitable and which may explain the improvement, but these desirable changes are not easily secured without the housing program.

PARTICIPATION OF PRACTICING PHYSICIANS

During the late twenties there was evident in many communities a determination on the part of public health authorities to achieve certain goals, as for example, the immunization of the child population or the examination of the preschool children, by reliance upon publicly supported agencies. This policy was never prosecuted to the point of serving adequately the child population or of closing a fruitful field to the private practitioner, as the White House Conference survey[24] clearly demonstrated. It was nevertheless carried beyond the stage of demonstration and offered to many who might better have turned to their personal physicians. The economic difficulties of the early thirties have operated to correct this trend. The restriction of public health funds has in many instances forced the health officer to relinquish routine services and to look upon himself as a champion and promoter of these services rather than their provider. On the other hand, economic conditions and the low incidence of illness have made preventive health procedures seem more worthy of cultivation to practicing physicians. The same forces have, however, increased the proportion of those unable to pay for preventive procedures. As a result, there have been many evidences of cooperation between departments of health and local medical societies in work directed toward the establishment of more satisfactory relations, and especially toward a greater participation by private practitioners in broad health movements.

An article by the Bureau of Medical Economics of the American Medical Association[25] discusses a number of local movements and indicates their wide divergence in method but their common purpose.

Space does not permit a consideration of the effects upon child health services of the various plans now in operation, or the direction

of trends in different communities. So far as they strengthen the ties between the personal physician and the family, and increase rather than diminish the acceptance of the important health procedures, these changes may be accounted evidences of progress.

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American Academy of Pediatrics

Proceedings

FOURTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

JUNE 11 AND 12, 1934

Panel Discussion on the Ductless Glands

Leader: R. G. Hoskins, M.D., Boston, Mass. Assistants: C. A. Aldrich, M.D., Winnetka, Ill.; J. B. Collip, M.D., Montreal, Que.; Murray B. Gordon, M.D., Brooklyn, N. Y.; Henry F. Helmholz, M.D., Rochester, Minn.; Irvine McQuarrie, M.D., Minneapolis, Minn.; A. Graeme Mitchell, M.D., Cincinnati, Ohio; E. Kost Shelton, M.D., Santa Barbara, Calif.; and Fritz B. Talbot, M.D., Boston, Mass.

The Panel Discussion on Ductless Glands was called to order at 11:30 A.M. by R. G. Hoskins, M.D., Harvard Medical School.

CHAIRMAN HOSKINS.—There is something new abroad in the land known as "progressive education." I know little about the progressive educators, but they have introduced into American educational circles the so-called "panel discussion." The idea of the panel discussion is to get together a group of people, preferably people who have had some experience and ideas on some problem worth discussing and have them "thresh out" the subject in public.

As the idea comes into medical meetings, it seems to encounter a serious difficulty: everyone wants to make a set speech; that is contrary to the spirit of the panel discussion. We shall aim to interrupt by impertinent questions any man who starts going too strongly on such a bent. It is part of the technic of the panel discussion to have questions come in written form from the audience. If time and ability of the group serve, we shall undertake to answer any questions that are thus presented.

(The members of the group were introduced.)

Dr. Shelton claims to have no competence as a pediatrician and comes before you strictly as an endocrinologist. Apropos to his claim of knowing nothing about pediatrics—he practiced medicine in a Colorado community for seventeen years—delivered babies, treated epidemics, served as guide, counsellor and friend to the community for a hundred miles around. I don't know whether they had pediatrics in that community but, if they did, Dr. Shelton was the man who supplied the pediatrics.

The next man in the group is Dr. Irvine McQuarrie, professor of pediatrics at Minneapolis. It would be impertinent on my part to introduce him to this audience.

Professor Collip is professor of biochemistry at McGill. He is the first man, so far as I know, to have successfully organized research in physiology on a wholesale plan. His work on insulin and on "parathormone" is known to all of you.

The interlocutor on the program has, for a number of years and in a fairly inoffensive way practiced physiology. In the meanwhile, for the past half dozen years, he has been practicing what, I suppose, could best be characterized as research psychiatry. (Dr. Helmholz, Dr. Mitchell, and Dr. Gordon were then introduced.)

I have asked Dr. Helmholz to open the discussion by presenting the general subject of endocrinology as it appears to a pediatrician who says he does not know much about endocrinology. He is going to survey for you the field as it looks to the pediatrician. We are in a very peculiar position in this country, economically and scientifically. Economically we are surrounded with great abundance—shoe factories that can make twice as many shoes as we can use; 50 per cent more farms than we can use. Half the farmers in this country, practicing agriculture as they do, could feed everybody in the country. We have an abundance in the mass and scarcity among individuals. Our problem of distribution is a trying one, sadly in need of a much better solution. We are in a good deal the same situation in physiology, and particularly in endocrinology. We have in endocrinology, at the present time, a vast amount of perfectly substantial, well-authenticated material, most of which has not yet got into circulation among the men who can make practical use of it. A good deal of this is still in the form of raw material which will have to be "processed" before it can be put to actual clinical use.

DR. HELMHOLZ.—The topic assigned to me is relatively simple because it is limited to a discussion of those disturbances which have been proved to be due to hyperfunction or hypofunction of a gland of internal secretion, and for which the appropriate hormone is available for general use or for which surgical interference is possible. I shall discuss only those endocrine disturbances, controlled investigative studies of which have been carried on over a sufficiently long experimental period to make possible a routine of treatment that can be carried out by the pediatrician.

A great many endocrine products have been placed on the market without adequate control and have been recommended for numerous types of dysfunction; some of these products, in which the active principle has been isolated only in the last few years, are not yet ready for use by the practical pediatrician. It is about this latter group that most of our attention will center this morning.

It is my present opinion that there are just three hormones concerning which investigation has been sufficiently controlled that they can be unreservedly recommended for use in pediatric practice. I refer to the hormone of the thyroid gland, thyroxin, that of the pancreas, insulin, and that of the posterior lobe of the pituitary gland, pitressin.

The thyroid hormone was isolated in crystalline form by Kendall. Thyroxin must be given intravenously and, on this account, has not displaced the desiccated gland in the treatment of thyroid hypofunction. Clinical manifestations of thyroid deficiency depend on the age at which the condition develops. If the condition is congenital, the typical picture of cretinism soon becomes evident. Reserves of thyroid secretion from the mother delay the manifestation of insufficiency until the child is from three to four months old. The picture of deficiency is so characteristic that it should not be mistaken for anything else. If the patient has normal thyroid secretion for a few months, and then, as a result of infection or some other factor, the thyroid gland ceases to make thyroxin, infantile myxedema develops. If destruction of thyroid tissue comes after years of normal secretion, the juvenile type of hypothyroidism develops. The earlier insufficiency develops and persists during the first two years of life, the less likelihood is there of normal mental development, in spite of normal physical growth. Early diagnosis and administration of thyroid hormone is most important.

In a series of about 157 cases of exophthalmic goiter encountered at the clinic, the metabolic rate before operation averaged +47 per cent before the use of iodine; since iodine has been given, the average metabolic rate before operation has been reduced to +16 per cent. The mortality rate, which was about 5 per cent before the institution of treatment by iodine, has been reduced to less than 2.5 per cent. Of those patients who were not operated on, two who refused operation died within a year. Geographic situation apparently plays a large part in the severity of this disease, which fact becomes evident when one compares the figures from the region of the Great Lakes with those of the Atlantic seaboard.

The use of insulin in diabetes is so standardized that at present it can be used by anyone who can carry out routine examinations for sugar and who can prescribe a weighed diet. Some have gone so far as to prescribe a regular diet and to control glucosuria by sufficient administration of insulin. The clinical entity, hyperinsulinism, which condition is the result of tumor of the islands of Langerhans, is now generally recognized. Not so common as hyperthyroidism, it nevertheless is a definite condition, which can be cured by surgical removal of the pancreatic tumor. The relation of the hypoglycemia to convulsive disorders is of special interest to the pediatrician.

A third gland which gives well-recognized symptoms of both hypofunction and hyperfunction is the parathyroid. What relationship there is between hypofunction of the parathyroid gland and infantile tetany at present has not been determined. That the parathyroid gland may play an intermediary part seems probable. Marked hypertrophy of this gland in experimental rickets of chickens is evidence of the effect. Infantile tetany, as well as idiopathic tetany of older children, is at present not permanently controlled by parathyroid extract, and they seem to recur after a period of return to normal. Hypersecretion of the parathyroid gland has been shown to produce a great variety of clinical symptoms, most outstanding of which are hypercalcemia, and hypophosphatemia and hypersecretion in the urine of both calcium and phosphorus. The disease of bone, osteitis fibrosa cystica, and simple osteoporosis without cysts, and renal lesions of different types are all the result of hyperfunction of the gland, usually caused by an adenoma. Successful removal of the tumor will cure the disease unless the kidneys have been too badly injured.

Crystalline cortin is also available at present, but Addison's disease is practically unknown in childhood, so that it does not concern us at present. Whether the syndrome of precocious sexual development, hirsutism, adiposity, and hypertension is due to excessive secretion of the gland is at present unknown; it is known, however, that removal of the suprarenal tumor will relieve the condition and bring about return to normal.

With regard to the use of pitressin nothing need be said. It is well known that diabetes insipidus can be controlled temporarily by the use of hypodermic injections of this substance.

The pituitary gland recently has been studied intensively, and new products have been produced which affect the pancreas and the thyroid, pituitary, mammary, and sexual glands. At present it seems advisable, from the point of view of the practical pediatrician, to await the results of carefully controlled studies before using such products.

With regard to the practical application of both insulin and pitressin, it is to be hoped that a better way of administering them will be found than by the hypodermic route, so that children will not be in constant fear of the hypodermic needle.

DR. McQUARRIE.—How would epinephrine be classified, as a drug or hormone?

DR. HELMHOLZ.—We use it as a drug rather than as a hormone. It has been used in Addison's disease very extensively with practically no results.

CHAIRMAN HOSKINS.—Dr. Shelton, what is your impression of the implication that hypothyroidism is a single entity?

DR. SHELTON.—Hypothyroidism can give rise to different clinical pictures. In the first place during the stage of development, one should think of the thyroid hormone as one of tissue differentiation. If the inherent destiny of the germinal protoplasm is interfered with, it is obvious that other endocrine glands would become secondarily involved. Thus the terminal picture would be a pleuriglandular one. There are many conditioning factors. Myxedema is only one symptom of the hypothyroid state, frequently a terminal one at that. The diagnosis of hypothyroidism should never rest on the presence of myxedema alone.

CHAIRMAN HOSKINS.—Hypothyroidism, as I conceive it, is essentially two different conditions. One is marked by a general lethargy, sluggishness of mentality and of metabolism. There is another type of hypothyroidism which, I think, is just as genuine an entity, in which the picture is not one of lethargy but of irritability. This, I think, Dr. Gordon might tell about.

DR. MURRAY B. GORDON.—There are two types of hypothyroidism in children. I take issue with Dr. Shelton on the term "myxedema." There is a great deal of confusion in the literature as to the term "cretinism" in this country. Cretinism is used interchangeably to designate endemic cretinism and sporadic cretinism, which some of us would rather call childhood myxedema. Cretinism is a condition due to endemic conditions and only partly due to hypothyroidism. As a result of a study of all the cases reported in this country, I feel that so-called cretinism differs from that seen in Europe in that it is due to hypothyroidism and is not endemic. Some of these children with deficient thyroid activity have myxedema, and some have not. In suggesting the term "childhood myxedema" about fifteen years ago, perhaps I was not correct in using the term for all the cases, but the original classification included both childhood myxedema and the hypothyroid state in children.

Hypothyroidism, or childhood myxedema, consists of two types: the first is the typical, fat, pudgy, lethargic child with myxedema or pitting of the skin; the second is the hyperexcitable child who is not fat and who does not present any myxedema. Both types have a low basal metabolic rate in addition to retarded carpal bone development, and both will show improvement following the administration of thyroid extract. You can compare the effects of thyroid extract in this type of case to the relationship between the effect of luminal and strychnine. A small dose of $\frac{1}{20}$ or $\frac{1}{10}$ gr. in the second type of child will have a sedative effect, and as the dosage is gradually increased over a period of months, a tolerance point will be reached, beyond which a large dose will produce hyperirritability. This latter dose depends upon the autogenous amount of thyroid extract present in the individual. These two conditions of myxedematous and nonmyxedematous hypothyroidism and the sedative and stimulative effects of thyroid extract must be considered in any discussion of the thyroid gland.

CHAIRMAN HOSKINS.—I think the practicing physician is prone to overlook the fact that in the thyroid substance we have, in effect, two drugs. It can have a pronounced anabolic effect, cause a child to grow as much as ten or twelve inches in a year, and serve as a general quieting agent; or it can be pushed hard and can become a "whip" agent. It happens, unfortunately, that thyroid is used largely for the whip effect when it is prescribed as a medicament for hypothyroidism.

DR. HELMHOLZ.—Some of the cases to which Dr. Gordon called attention have been diagnosed hyperthyroidism without exophthalmus because of the irritability

and the slight goiter, as it occurs in girls at about the age of puberty. We have seen a number of such cases that have come in as examples of hyperthyroids with basal rates of −24 to −30.

CHAIRMAN HOSKINS.—That group of patients is largely overlooked in general practice, and it is unfortunate because they respond to thyroid medication as well as the other type. It is rather curious that the irritable type of hypothyroidism has been so generally overlooked. In the classic report of the British Myxedema Commission in 1888, this aspect was strongly emphasized: the hypothyroid subjects studied showed all kinds of irritability even to psychoses in some cases.

Dr. Helmholz mentioned the fact that the use of parathyroid—"parathormone"—the father of which sits at my right, leads not infrequently to a condition of refractoriness. The patient ceases to react to that preparation. I would be glad if Dr. Collip would give us the rationale of why the material ceases to be active.

DR. COLLIP.—In the studies made during the past year in my laboratory on the various active principles of the anterior lobe of the pituitary, it was found that continuous treatment of experimental animals with certain hormones leads to the establishment of a state of nonresponsiveness on the part of the treated animal. It was shown that the blood of an animal resistant to the thyrotropic hormone was capable of neutralizing the effect of the thyrotropic hormone in a fresh test animal. Such results opened, so to speak, an absolutely new vista in endocrinology.

The point Dr. Hoskins has made is important. It has been well known for a long period that an animal or patient treated with parathyroid extract known to be potent shows in a short time in some instances, and in other cases after a longer time, an apparent resistance to this hormone.

In the short time at my disposal I should like to say something about the principle of inverse response and the theory of antihormones and to make it clear that my recent pronouncements on these topics were of a theoretical nature. The theory had its birth in our laboratory, because of certain proved facts. This theory may be incorrect in many ways, but it is hoped that it will act as a stimulus to further work. The laboratory worker is often accused of being impractical, but here one may perhaps see a bridge from the laboratory to the clinic, since the antihormone theory can be applied quite as well in the clinic as in the laboratory. To be more specific, we found, with Dr. Anderson, that animals treated for many days, weeks or months with an extract of the anterior pituitary lobe of the ox, pig, or sheep purified so that the active principle which has a specific stimulating effect upon the thyroid gland was being administered in concentrated form, showed in the first instance an elevation of the metabolic rate. In the course of a few days, however, the metabolic rate returned to normal, and as the experiment was continued the metabolic rate fell to −30 per cent of normal, which is the level of metabolism of the hypophysectomized animal. During the period of elevation of the basal metabolic rate, definite evidence of hyperplasia of the thyroid gland was obtained, but after the metabolic rate had fallen to subnormal values, the thyroid gland was diminished in size and quite comparable in its histologic appearance with the resting gland of the hypophysectomized animal. Here, then, we had what at first appeared to be a peculiar, if not ridiculous situation. The administration of a highly purified hormone extract, which one felt represented a very positive stimulant to the thyroid gland, actually produced, after a short period of definite stimulation—shown both by the elevation of the metabolic rate and by the histologic appearance of the thyroid gland—a state of hypothyroidism comparable to that seen in the hypophysectomized animal.

We found that the serum of these chronically treated animals resistant to the thyrotropic hormone was capable of neutralizing completely the thyrotropic hormone when the experiment was carried out on the most sensitive test object, the recently hypophysectomized rat. At first we were naturally inclined to think that we were probably dealing with an antigen-antibody reaction, since the hormone extracts used contained protein. Other experiments, however, which I cannot take time to describe, suggested the possibility that we were dealing with a true antihormone; and the possibility had to be considered that the antihormone or antagonistic substance is present all the time, and that our experimental results could be explained on the assumption that we had raised the level of a substance which was already present in the blood. A theoretical concept which follows from this is somewhat as follows: for each hormone there may be an antagonistic or antihormone, and the stability of an individual as regards any particular endocrine aspect may depend upon the balance between the hormone and the respective antagonistic substance. One might even look upon this hormone-antihormone complex as a "buffer" system. In this way one might introduce a very definite quantitative aspect to the theory. It is not possible, of course, to detect the hormone and its antagonist simultaneously, since one or the other must predominate.

CHAIRMAN HOSKINS.—The principle Dr. Collip introduced, I think, is revolutionary. It is going to necessitate the rethinking of the subject matter of the whole field. Before, we had to deal, for instance, with only thyroid excess or thyroid deficiency but now we have had introduced the complexity of an antithyroid substance, apparently just as normal as the thyroid hormone itself. This finding materially complicates the philosophy of the situation.

There must have occurred to all of you the significance of this principle when it comes to practical therapy. If you put a baby on thyroid, for example, and he promptly begins to develop antithyroid principle, you are limited as to how far you can go. Perhaps Dr. Collip will discuss the possibilities that lie before us in overcoming the handicap which the existence of antisubstances sets up. Parenthetically, I am inclined to believe Dr. Collip has put his finger on the reason why so much gland therapy has been futile in the past.

DR. COLLIP.—If this work develops along the line it is pointing, it is really a very serious bombshell thrown into endocrine therapy, but it should not be entirely destructive. We should be able to treat patients much more rationally. To give an illustration, it is feasible that the case which you clinical men rightly diagnose as manifesting a hypofunctional state of A, B, or C gland is perfectly normal so far as the production of a particular hormone is concerned, but the trouble may be that there is too much of its antagonist. It may be that one gland produces both the positive substance and the negative substance, or it may be that the antagonistic hormone is produced somewhere else. But my point is that there is in the normal a balance between positive and negative in regard to individual hormones. If, for instance, you have a hyper-antihormone state, that state may be recognized by actual experimental demonstration of the antagonistic substance in the blood of the patient.

My plea is not that we give up treatment but that we study the patient from the standpoint of the hormone content so far as reliable methods are available. We have been experimenting along clinical lines with some of the pituitary fractions, which we know now produce in rats, horses, dogs, goats, rabbits, and guinea pigs a hyper-antihormone state in these respective animals. Such extracts given to patients have led to similar results. We have been able to detect the antihormone for the thyrotropic substance in the blood of patients whom we have injected with this hormone. I may say the case which Dr. A. D. Campbell demonstrated yester-

day in his lecture actually has this antisubstance. It may be a good thing to produce a hyper-antihormone state but let us find out whether we want to produce a hyper-antihormone state or hyper-hormone state before we start treatment.

The principle of inverse response is well illustrated if we compare a normal guinea pig with a normal rat. The guinea pig, as is well known, is highly sensitive to thyrotropic hormone of the anterior lobe. A small amount of this principle given to a guinea pig produces slight hyperplasia of the thyroid within a matter of hours, and after three days marked hyperplasia, together with a definite elevation in the metabolic rate; whereas the normal rat is practically insensitive to administered thyrotropic hormone. If you take the pituitary of the guinea pig and determine the amount of thyrotropic hormone in it, you will find it is very small, almost negligible. If you determine the amount of thyrotropic hormone in the pituitary of the rat, you will find that it is rich in this principle. I could go on giving other examples. Since the rat has a lot of thyrotropic hormone in its pituitary and is relatively insensitive to administered hormone, the principle of inverse response becomes evident: that is to say that the responsiveness of an individual to administered hormone varies inversely with the hormone content or production of the individual's own gland.

CHAIRMAN HOSKINS.—That sounds like something new. Dr. Collip, I know, from personal conversation, recognizes the fact that this is something comparable to the old Weber-Fechner law we all had to learn in physiology. If 50 pounds of weight are resting on the back of your hand and you put an additional ounce on the pile, you feel no difference. However, if you have a 0.5 gram weight to start with and put on the same addition as before, you appreciate a very marked increase in the weight. The same principle, I think, holds here. If your patient is circulating hormone at a low level, the addition of a little more hormone makes a significant difference. If he has a lot there already—and especially if it is buffered by antihormone—the addition of a considerable amount more makes relatively little difference. This is extremely interesting as endocrine philosophy. I think this audience, however, will be more interested in what we know empirically as to how we can overcome this sort of handicap. Dr. Shelton, this principle that Dr. Collip has enunciated presumably has been operative during all the time you have been using practical gland therapy. How do you think you have circumvented it in the actual treatment of the patient?

DR. SHELTON.—I don't know that we shall be able to circumvent it. There are several clinical arguments for the theory and several against it. In the first place, it is well known that some individuals with hypothyroidism or myxedema are very sensitive to desiccated thyroid administration. One may interpret this as meaning that those susceptible have few, if any, antibodies to this particular hormone. An individual with the thyroid gland surgically removed or otherwise destroyed is frequently susceptible to the hormone and may tolerate only a small dose of desiccated thyroid. Likewise I have seen normal individuals or so-called borderline patients who could take enormous doses of thyroid without elevation of the basal rate. In administering pituitary growth hormone, we have noticed that children seem to respond rapidly at first; then the response tends to continue on a plateau. Even when the dosage is augmented, the increase in weight and height does not keep up in direct ratio to the additional amount of the hormone introduced. However, we feel that perhaps this antibody effect may be circumvented by allowing a certain amount of time to elapse between periods of treatment. In other words we may learn that a period of treatment and a period of rest is better than continuous treatment.

One of the children we have had under treatment for two years grew 5.4 inches on the growth hormone; growth practically reached a plateau at the end of this time. While she was away in her home in Honolulu, without treatment, she grew only 0.7 inch in thirteen months. Since she has returned, we have resumed administration of the pituitary fraction. She has grown approximately one inch in three months. I realize that the product we are using is an imperfect one, perhaps containing the sex fraction and the thyrotropic and adrenotropic fractions as well as the growth. If our little patient has become refractory to any of these, however, we are not aware of it. The fact remains that after a rest she has grown more on treatment during the past three months than she grew without treatment during the previous thirteen months.

CHAIRMAN HOSKINS.—There is an old empiric rule that probably half unconsciously has been based on this principle. It has been believed by shrewd practitioners that one gets better results, on the whole, by intermittent medication than by continuous medication. That always seemed a rather stupid sort of arrangement, but I think we have here a rationale which makes it seem highly intelligent practice.

There will be other questions coming up in relation to the pituitary as the discussion proceeds. It is an important gland, perhaps the endocrine motor of the whole system. A baby cannot develop normally in utero without normal pituitary potations which he derives first from his mother and later from his own gland; he cannot go through infancy in a normal way without pituitary substance. He needs it through childhood; and when he comes to the adolescent period, he is completely unable to make the normal transition without a functioning pituitary.

From the practical point of view, the gland gets into every situation with which the pediatrician has to deal. Whether or not he recognizes its presence, it is there as an important factor in the total life-situation of the baby—both physically and mentally—and probably as an important factor in personality. I hope that we shall have time to go back to some of these points.

Reference has been made in one or two places so far in the discussion to the parathyroid glands. Dr. McQuarrie has been thinking about these glands for some time, and I would be glad if he would take up the discussion at this point in relation to the practical aspects of the parathyroid as a contributor to welfare or "ill-fare."

DR. McQUARRIE.—I have been thinking about the parathyroids and the possible application of the theory in clinical conditions showing disturbances in the functions of the glands, namely, in the states of hypofunction and hyperfunction. We encounter idiopathic parathyroid tetany frequently, and, while the condition is not common, every one has had some experience with such cases as well as with infantile tetany, which might be related. During recent years many cases have been encountered, some of them in children, of hyperfunction of the glands due to tumor in some instances, or to glandular hyperplasia in others.

I have wondered, since hearing Dr. Collip's paper in New York before the Federated Society a few months ago, whether our cases of idiopathic parathyroid tetany may not, in some instances be due to overproduction of some antisubstance. Again in the hyperparathyroid cases with hyperplasia, do they represent one phase in the reaction to this mechanism? Have some of the hypoactive cases gone through a hyperactive phase? We have all sorts of possibilities before us in the light of this new work.

Just as we have diabetogenic and thyrotropic substances in the anterior lobe, Hertz and Kranes, of Boston, have recently discovered a parathyrotropic substance, a substance which when injected into animals produces very definite hyperplasia of

the parathyroid glands, that is, an increase in the number of parathyroid cells, enlargement of these cells, and probably hyperfunction as well.

While any clinical applications will be experimental for a long time, in one of our patients with so-called idiopathic parathyroid tetany, we have injected daily for a week at a time some anterior lobe extracts already available to us in the hope that these might possibly contain some of the parathyrotropic substances which would tend to have a stimulating effect in such patients. Since the first experiment was not entirely satisfactory, we are repeating it the second time. The first study has shown that the calcium and phosphorus excretions are increased as they are in hyperparathyroidism. The calcium and phosphorus of the blood have not so far responded as one expects them to on administration of the parathormone or in the presence of hyperactivity in the case of tumor or of hyperplasia of the gland, but it is suggestive and certainly our approach to the subject seems justifiable in the light of Dr. Collip's new hypothesis.

I would like to say in connection with this that refractoriness or immunity which is produced in hypoparathyroid patients when they receive the parathormone over a long period of time may be due to one of several factors which one could correct or avoid. In addition to the occasional interruption of therapy already referred to, the factor of dosage is very important. It is remarkable how sensitive these individuals are to small doses of parathyroid substance, at least at the beginning. This fits in well with Dr. Collip's theory, I think. Minimal effective dosages should be established for each case and then adhered to. Diet is another factor in this particular disturbance at least. When the patient is getting a high calcium and phosphorus diet, less hormone is required. The ratio of the calcium to the phosphorus in the diet, the total base and acid in the diet, and the hydrogen ion concentration or acid base equilibrium in the body fluids, influence the activity of the gland very much. These factors certainly should be taken into consideration. We should do everything we can with vitamin D, the acid base balance and high calcium in the diet without depending entirely upon the parathyroid extract. Then, by giving the patient small doses from time to time, we can at least extend the period of usefulness of that hormone.

The child who has hypofunction of the parathyroid certainly is an irritable individual. Whether this condition is due to increased brain cell membrane permeability or to some other fundamental disturbance in cellular physiology, he is very irritable and shows increased muscular tonus. According to some recent work, there is an increase of water contained in the brain tissue in the state of hypoparathyroidism. Under such conditions the cortical cells perhaps behave abnormally, as do the other cells of the body.

In the hyperparathyroid state the individual is less responsive. There is a lessened neuromuscular irritability. He is hypotonic. He may be irritable from pains in the bone due to tumor growth or cyst formation and to some changes in the muscles, but he is not hyperirritable in the sense that the hypoparathyroid patient is. I can say, from the personality side, therefore, that this change in physiologic state makes a basis for disturbances in personality reaction. Mental reactions beyond that I know nothing about. You know so much more concerning this aspect of the problem that I wish you would tell us about it.

CHAIRMAN HOSKINS.—May I ask Dr. Collip to interrupt Dr. McQuarrie. What is there in this idea that, as we give parathormone with a hypodermic needle, we are a long way from imitating the way nature gives it to the patient? We give at a single dose what may amount to several hours' normal supply. When this is used up, the patient sinks into a trough of total deprivation. Then we give him another "bump." Possibly all the peaks in the dosage stimulate the production

of the antisubstance. I should like to know what Dr. Collip thinks of this. Instead of setting up this "up-and-down" situation, we should try as nearly as feasible to carry the patient along on a plateau of dosage and at as low a level as will suffice.

DR. COLLIP.—The more frequently an extract is administered and the smaller the individual dose, the nearer you are approaching ideal conditions. But, of course, there are obvious limits to this. One would like to know, for instance, if this were carried out as far as possible, whether by the reduction of dosage and by the increase in the frequency of injections, this antihormone response would be avoided. In nature the absolutely normal individual's various glands are pouring out hormones continuously at a certain definite rate. It may be normal for one species of animal to have a slight predominance of the antisubstance whereas another has a predominance of the positive. I have no absolute proof of this, but I feel that the reason a dozen dogs can be killed with the amount of parathyroid extract one rabbit will thrive upon is a good illustration of this principle.

CHAIRMAN HOSKINS.—I think we have to assume this mechanism is not put in just to make trouble for the endocrinologist. But it is sound, as furnishing a lead at any rate, to try to deduce what the ultimate significance of the mechanism is in the evolutionary process. We shall have to assume at this stage that it is a protective device to prevent the individual from overdosing himself with his own hormone under the vicissitudes of life. We shall also have to assume that there is a balance, ordinarily, so that this regulating mechanism does not defeat its own purpose. A governor on an engine that shuts off steam when you want the engine to be pumping would be a poor sort of governor.

It is necessary to assume that the antisubstance comes in only when the hormone rises for some special reason too high and has to be corrected, so to speak. An important aspect sometimes overlooked is the fact that the individual is not just a collection of adrenals and thyroids and stomachs and colons and things of that sort, but a person with the personality that gives this "mess of viscera" its meaning. That topic, I think, could be touched upon with profit by Dr. McQuarrie. He told about the tendency to tetany, which is very interesting as physiology, but what about these conditions in relation to personality? What difference does it make to the personality of the youngster? How much more does the mother have to stay up nights with him because of his parathyroids? The influence it has on personality is the most important part of endocrinology. Unfortunately, we have been rather extensively indoctrinated on the "influence of glands on personality" but the "doctrine" is sadly lacking in factual support. Nevertheless, despite the abuse the topic has had at the hands of reportorial scientists, it is still an important topic.

There is one gland which, according to Riddle, probably dates back in importance to the preterrestrial stage of our ancestral history—which has permitted us to gather for this delightful occasion today and without which our ancestors would have perished from the earth—a gland which has been a paradox, especially to pediatrists. I am referring to the thymus gland, the subject of Dr. Graeme Mitchell's talk.

DR. MITCHELL.—While the subject of endocrines should, because of the interrelationship of the various secretions, be considered together, there are individual interests concerning each of the so-called glands of internal secretion. In approaching the subject of the thymus gland, I wish to make clear that I am interested in it as a clinician who is faced daily with the attempt to solve the problem as to what should be done in instances in which this organ possibly, either by pressure or by some other mechanism, causes symptoms.

Opinions concerning the thymus have, like the pendulum, swung from one end of the arc to the other. Recently some pediatrists, whose opinions must be regarded with respect, have intimated that the thymus gland never causes symptoms. In such a controversy it would appear from a philosophic point of view that the truth might lie somewhere between the extremes.

The literature on this subject is cluttered with a good deal of material based upon erroneous or unjustifiable presumptions regarding the pathology, physiology and functions of the thymus gland. Those who have studied the subject experimentally by observations on animals after the thymus has been removed or by injecting extracts of it into animals have often urged opposing opinions. There arises, too, the difficulty of translating to the human the results of experiments on animals since it is possible that the organ may have different functions in different species.

I have made a mathematical analysis of a group of patients, some of whom had enlargement of the thymus gland according to roentgenographic interpretation.

For example, 197 patients could be divided into four groups. Eighty patients had enlarged thymus and symptoms; 36 had enlarged thymus but no symptoms; 43 patients had no enlargement of the thymus but did have symptoms which are often attributed to the thymus gland; and last, there was a comparative group of 38 patients without enlargement of the thymus gland and without symptoms. This allowed analysis by means of the fourfold table and gave a sigma of 2.26—the mathematical implication being that these four groups come from the same universe or, in other words, that the symptoms mentioned (stridor, cyanosis, and convulsions) were not inevitably associated with enlarged thymus.

If these 197 patients were divided into two groups, it was found that 116 had enlarged thymus according to the roentgenograms and eighty-one did not. Of the former group, 69 per cent had symptoms, and of the latter group, 53 per cent. Applying the chi-square test the sigma was 6.39—that is, these two groups had not come from the same universe, and the symptoms mentioned, therefore, are more likely to be associated with enlarged thymus.

Of 80 patients who had enlarged thymus, there were 56 who had complicating conditions (congenital heart disease, respiratory infection, and increased intracranial pressure) which might equally well have been responsible for the symptoms. That is to say, there were only 24 patients in whom some other cause could not be discovered for the symptoms. Applying statistical analysis to these two groups it was found that the sigma was 4.47 and that the rate of incidence of symptoms was higher in patients with enlarged thymus who had other reasons for these symptoms than in those patients who had only enlarged thymus. The implication here is that a child with an enlarged thymus and some complicating condition such as those mentioned is more liable to have symptoms than one with an enlarged thymus only.

It is interesting that of 116 patients with enlarged thymus 20 had pylorospasm, whereas, of 81 patients without enlarged thymus 33 had pylorospasm. That is, from a statistical viewpoint, there is no obvious association between enlarged thymus and pylorospasm.

CHAIRMAN HOSKINS.—May I interrupt Dr. Mitchell to extend my heartiest congratulations to him for having brought into his work an accurate calculation of probability. We deal with things in medicine all the time which are probably true or probably not true. There are a great many open questions. I think it is a definite advance that we are beginning to calculate as accurately as can be done just what the odds are that a given assumption is true and what the odds are

against it. We can judge better if we know the odds are, for instance, 20 to 1 in favor of the assumption than if we know only that there is some probability that it is true.

What do you think, Dr. Mitchell, of the remarkable work on the thymus that has recently been reported from Philadelphia?

DR. MITCHELL.—Dr. Hoskins previously called my attention to the recent work of Dr. Rowntree in which there was remarkable accelerated growth and development in rats injected intraperitoneally by a thymus extract made by Hanson. If continuation of this work properly controlled bears out the original observations, much significance can be attached to it.

CHAIRMAN HOSKINS.—We have been giving extracts to rats for a great many years, and nothing has ever before been seen like a rat being weaned at three days of age or giving birth to young at forty-two days of age. Such precocity is as startling as would be that of a little five-year-old girl giving birth to twins. That sort of thing is out of the biologic picture as we have known it before. Dr. Rowntree's pictures are convincing in that rats four days old were seen running around with coats of fur while normal rats raised under the same conditions but without the thymus extract could only waddle awkwardly about as little pink "blobs."

DR. MITCHELL.—I am going to recite to you certain viewpoints rather than conclusions, which summarize my present views on the thymus. It appears that some of these statements can be made with a reasonable amount of assurance.

In some instances an enlarged thymus gland can cause pressure upon the structure in the thoracic inlet and lead to development of such symptoms as dyspnea, suffocative attacks, crowing respirations, cough, and cyanosis. The symptoms mentioned occur with many other diseases and abnormal conditions, and these are perhaps more frequent causes of all of them than is an enlargement of the thymus.

An infant or child who has some cause for dyspnea, cough, and cyanosis, such as an infection of the respiratory tract, congenital heart disease, and the like, and who also has an enlargement of the thymus gland is more liable to develop these symptoms. Probably the enlarged thymus may aid in their production, but in some instances it would be a factor which would be insufficient in itself to cause such symptoms.

From a statistical point of view there is no significant association between an enlarged thymus and pylorospasm.

There is no proof that convulsions are associated with an enlargement of the thymus gland, and the presence of convulsions even in a patient with an enlarged thymus gland should lead to a suspicion that there may be increased intracranial pressure, spasmophilia (tetany), or some other cause.

An enlarged thymus gland according to roentgenograms is by no means necessarily associated with symptoms.

Even when symptoms of obstruction are present in an infant or child with an enlarged thymus, search should be made for other possible causes.

I have no solution to the question of the relationship of sudden death, when not explicable by some discoverable cause, to status thymicus lymphaticus.

CHAIRMAN HOSKINS.—Dr. Riddle called our attention to his belief in the importance of our ancestral thymus gland. If a few million years ago it had gone out of the picture, we should not have come into existence. There is another gland, the function of which is such that if it had not appeared in our individual pictures about the time we drew our first breath we again should not be here. I have asked

Dr. Gordon to talk to us about the adrenal gland and its relation to practical pediatrics, and perhaps to touch upon its function in getting us past the intrauterine course of existence into the postnatal phase.

DR. GORDON.—Before going on to the discussion of the adrenals, I would like to speak about the thymus. The question of the physical condition of the thymus must be absolutely differentiated from the endocrine aspect. We feel that there is no definite physical knowledge as to the size of the thymus at various ages in infancy and even at the same age in various children. It tends to be larger in stout, well-developed children and smaller in the undernourished and thin. Information as to the size of the thymus by means of x-ray pictures may not always be exact, as the shadow is larger during inspiration than during expiration, the stage of respiration in which the picture was taken is, therefore, of vast importance in judging the size of the gland. Fluoroscopic examination offers more information than one isolated x-ray plate. One of the important steps in interpretation of signs and symptoms of thymic enlargement is standardization of the methods used in making roentgenograms of the gland—Pancoast's work should be studied by every one interested in this part of the subject. As to the endocrine aspects—most of us had dropped the thymus as a gland of internal secretion, but the recent work of Rowntree, Jaffe, and others may bring it back into endocrinology. In connection with the effects of thymic extract, I wish to refer to the limited experience that I have had with thymocrescin in two cases of anterior pituitary deficiency of growth. The patients were both boys, one seven and the other seventeen years old. We were unable to observe any effects on the height in either one after several months of treatment. It is probably unfair to judge the effects of the extract in the older boy as his epiphyses were almost united.

There are several aspects of the adrenal which I should like to discuss. The first is the part which the adrenal gland plays in the transition from prenatal to postnatal changes especially in respiration. It has been known for some time that the adrenal gland is very large before birth and that this increased size is due to the large adrenal cortex. Immediately after birth there is a degenerative change taking place in the adrenal cortex; this process goes on rapidly for the first week and then at a lower speed for the first year. It takes about two years before the medulla is absolutely differentiated, so that the conditions in antenatal are entirely different from postnatal life. We also know that in antenatal life there is a low oxygen tension, a low oxygen saturation of the blood, and that in spite of this the utilization of the blood by the fetus is much greater than by the mother. Animal experiments have shown that the responsible factor is the adrenal cortex. We cannot go now into what these animal experiments have been, but it seems that the size of the adrenal cortex is an indication of the effect of the adrenal gland upon tissue respiration and that, upon the birth of the child with the intake of a large amount of oxygen and the increase in oxygen tension, the adrenal cortex degenerates. This demonstrates that a large adrenal cortex is not necessary after the onset of pulmonary respiration.

Anything which would interfere with the normal interchange of oxygen should show a persistence of fetal conditions. This has been demonstrated clinically in two conditions. Dr. Goldzieher found at autopsy an absence of adrenal cortical involution in three cases of transposition of the great vessels with septum defect and marked cyanosis in infants of an age at which involution should already have occurred. Goldzieher and I found that an increased respiratory rate is so prominent a symptom in adrenal hemorrhage of the newborn that we suggest the term "pseudopneumonia of the newborn" for this condition. This is due to an attempt of a damaged adrenal cortex to adapt itself to the new conditions present at birth.

The diagnosis of adrenal hemorrhage is difficult, and we found that only eleven cases have been diagnosed during life out of the eighty-one in the literature. Goldzieher and I have advanced the following syndrome of adrenal hemorrhage in the newborn with two groups of symptoms: those due to acute adrenal insufficiency and those produced by internal hemorrhage. The symptoms of acute adrenal insufficiency are: The infant presents the appearance of pneumonia without any physical or x-ray evidence. There are present increased respiratory rate, hyperpyrexia, cyanosis, purpuric or petechial spots, and certain definite chemical changes in the blood, the principal ones being hypoglycemia and an increase in nitrogen metabolites. The symptoms of the nonendocrine elements are those of any internal hemorrhage such as shock, collapse, weak and irregular pulse, cold extremities, air hunger, and increasing pallor. These are especially marked if the hemorrhage is extensive and may overshadow the symptoms of adrenal insufficiency. The abdomen is doughy to the touch, and there may be a palpable tumor in one or both kidney regions.

Either set of symptoms may predominate and give the different types of pictures which have been reported. For instance, Arnold reported his case from the viewpoint of an internal hemorrhage alone while others have reported from the viewpoint of acute adrenal insufficiency.

Adrenal hemorrhage may occur in other conditions in later life as in the course of acute infections and may present the same set of symptoms as found in the newborn except that the respiratory rate is not as greatly increased.

The next condition of importance is that of acute adrenal insufficiency. There seems to be a lack of appreciation in the literature as to the difference between acute adrenal insufficiency as exemplified in adrenal hemorrhage and chronic adrenal insufficiency as exemplified in Addison's disease. In one we find an acute process taking place rapidly, and in the other we find a condition which has spread over a number of years in older children in whom there have been metabolic adjustments, especially to other glands of internal secretion; there the two pictures are entirely different. In acute adrenal insufficiency there are the same symptoms as in hypoglycemia, high nitrogen metabolites, and perhaps an increase in respiratory rate and high temperature. In chronic insufficiency the picture is really one of Addison's disease with a history of tuberculosis in either the patient or his family. Bell has recently shown that an x-ray diagnosis of the latter may be based on the presence of calcified glands in the region of the adrenal gland.

In acute adrenal insufficiency, as in adrenal hemorrhage, we have advised treatment from three approaches: first, the administration of a potent adrenal cortical extract such as cortin, interrennin, eschatin; second, the administration of large amounts of sugar either by intravenous injection or by hypodermoclysis; third, blood transfusion of an adequate amount. In chronic adrenal insufficiency, the administration of a potent cortical extract is important as shown by Rowntree. The use of glycerin extracts by mouth as advocated by Hoskins and Freeman may be of some benefit, as will the ingestion of food with sufficient vitamin content.

The adrenal gland seems to have a definite influence on sex. It has been shown, but not definitely proved, that hyperplasia of the adrenal cortex during fetal life results in pseudohermaphroditism. Hyperplasia or neoplasm of the adrenal cortex during infancy or childhood produces precocious puberty. We were able to report a few years ago the fifth case in the literature of this condition as it occurred in a boy three and one-half years old. It is much more common in girls. Another type, found in females between the ages of thirty-five and fifty years and known as "virilism," is due to a neoplasm or hyperplasia of the adrenal cortex. In this condition, characterized by a tendency toward heterosexual changes, the individual

takes on the appearance of the male sex as evidenced by an increase in hair growth resembling that of the male, a change in voice, and perhaps even a change in psyche.

It is sometimes difficult to differentiate between obesity due to hyperadrenalism and that due to hypopituitarism. Lately the literature concerning instances of adrenal obesity in infants and children has increased. These children may show hypertension, hirsutism, and perhaps signs of precocious puberty and heterosexuality.

An increased activity of the adrenal cortex will be accompanied by an increased osseous development as shown by x-ray examination, especially in the wrist. We have not been able to find any references to giantism caused by overactivity of the adrenal gland. On the other hand, there is a condition known as progeria which is supposed to be accompanied by hypoplasia of the thymus, adrenal, and pituitary and is characterized by a marked infantilism and a senile facies.

CHAIRMAN HOSKINS.—I want to call to your attention the fact that one of the most difficult problems confronting the clinical endocrinologist is that of the relationship between the thyroid and pituitary. There is a group of clinical pictures in which it is not easy to decide whether the thyroid or the pituitary is at fault or whether both glands are coincidentally involved. Dr. Shelton will tell us something about the practical management of this very difficult question, how the distinction is made, and what can be done therapeutically.

DR. SHELTON.—I am not sure that I can tell you how to distinguish between these disorders, but after considerable study of osseous unfolding, we feel we have devised a method which is at least informative.

Dr. Gordon spoke about the advance in carpal development in children with hyperactivity of the adrenal cortex. We know that children grow in height and develop structurally at a rather definite rate. It has been shown by a number of observers that removal of the thyroid anlage in tadpoles retards metamorphosis into the frog. These tadpoles may be kept in the tadpole or embryo stage of development indefinitely. If fed thyroid or if a piece of thyroid tissue is later grafted under the skin, this tadpole will metamorphose and develop into a frog. Therefore, the thyroid hormone has much to do with tissue differentiation or tissue unfolding. We feel also that there is a remarkable difference between development as we know development and growth of the organism per se.

Most of the dwarfs whom we have been treating (considered as having a primary pituitary etiology) show normal or only slightly retarded bony development, while hypothyroid dwarfs and those not markedly under stature but presenting evidence of hypothyroidism show a very marked retardation in osseous development (unfolding). So I feel that the clinical differentiation, particularly by the roentgen ray, may rest on this point: namely, if the child is of fair to good height or even dwarfish and if coincident with this there is a markedly retarded osseous development, as evidenced by retarded carpal or other bony unfolding, the primary and essential difficulty is probably due to a deficiency of thyroid secretion. If, on the other hand, I find a child who shows little evidence of retardation or unfolding of somatic development and yet is small or dwarfish in stature, I feel that the thyroid is not seriously involved and look to the pituitary to being primarily at fault. As regards overgrowth or speeding up of development, I think I can say safely that hyperthyroidism will produce rapid osseous unfolding. I feel that anything which will speed up development in general, and by development I do not mean growth but only actual tissue differentiation or metamorphosis, will ultimately be reflected in the framework or the somatic make-up of the individual. Since pituitary ablation results in thyroid and adrenal cortex atrophy, and thyroid ablation results in a generalized slowing up of all body processes—including the pituitary—it is likely that

in every child suffering from abnormal deviation in stature or aberrant development, the etiology is complicated. In a sense all are pleuriglandular. It frequently becomes necessary, however, particularly for the sake of treatment, to ascertain the primary and paramount difficulty. There are many clinical points of dissimilarity, but to me, at least, the roentgenogram of the bony framework is the most informative.

CHAIRMAN HOSKINS.—Dr. Shelton, will you take this question that was submitted from the audience? "Is the pharmaceutic claim correct that thyroid extract is the only gland product that can be given by mouth and produce any effect?"

DR. SHELTON.—This is a difficult question, and I can answer it only in the light of my own experience. Many men of equal experience may have different views. The only purely endocrine preparation that I use by mouth, in children, is thyroid. Adrenalin and some ovarian preparations and placental preparations including emmenin, when given in large doses, have been shown to produce a moderate therapeutic effect. Dr. Hoskins has shown that large doses of a glycerin extract of adrenal cortex, by mouth, will increase the blood pressure in his schizophrenic patients from 15 to 25 mm. of mercury. I do not believe he has been able to produce this effect in a series of normal controls. Personally, I have given large doses of pituitary preparations by mouth over prolonged periods without ever having convinced myself that they had any therapeutic effect. It has seemed to make no difference whether the preparation was coated or not. These were controlled observations in which no other gland product was given. Many pharmaceutic houses make tablets containing various glandular preparations plus a little thyroid. These frequently produce certain beneficial effects, but it is quite likely the thyroid which does the work. In my estimation one should never give thyroid in combination with other preparations. If you suspect the patient of needing thyroid, give him thyroid alone. Other things may be added if desired for an experimental clinical test after the effect of the thyroid is measured. For the present, at least, it appears best to limit the administration of gland products, by mouth, in children to desiccated thyroid.

FOURTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

CLEVELAND, JUNE 11 AND 12, 1934

Round Table Conference on Adolescence

Leader: Dr. Borden S. Veeder, St. Louis.
Assistant: Dr. Sidney I. Schwab, St. Louis.

The Chairman opened the meeting with a discussion of some of the physical problems of puberty and adolescence. The variations in the chronologic development of the accelerated growth cycle of this period were pointed out and the failure of physical growth to parallel the age in years. The importance of skeletal age was emphasized. The development of medical problems on the basis of the unorganized growth was discussed, and also the tendency to fatigue and overstrain which accompanies it.

Dr. Sidney I. Schwab (St. Louis) continued the introductory remarks with a discussion of some of the psychologic phenomena of the period. The importance of

the adolescent as a social unit, the development of personal identity and awareness on the part of the adolescent, and the changing character of his thinking from conceptional to abstract were among these phenomena. As an approach to the subject, adolescence may be regarded as a final preparation to reach a social adjustment; and the failure to make this adjustment, as a result of innate constitutional characteristics, faulty training or environmental obstacles, leads to the adolescent problems and conflicts. In the study of the adolescent three things must be considered: the adolescent as a physical being with his growth and development, the adolescent as he behaves and reacts to his particular environment, and third, the content of his consciousness.

Dr. Harold C. Stuart (Boston) spoke of the necessity of restudying adolescents from the standpoint of metabolism, activity, sleep, diet, etc., on the basis of the individual spurt of growth rather than by chronologic age periods as has been done in the past.

The question of distinguishing simple problems, which should be handled by the pediatrician rather than the psychiatrist, from deeper problems potentially psychiatric in nature, was discussed by the Chairman, Dr. Schwab, Dr. Alvah Newcomb (Chicago), Dr. Stuart, Dr. Bert I. Beverly (Chicago), and Dr. George F. Munns (Winnetka, Ill.). Several illustrations of these differences were presented. It was agreed that this was largely a matter of medical education and necessitated emphasizing the importance of regarding the adolescent as an individual rather than a purely physical mechanism. The importance of early training as a matter of prevention was stressed, and hence the work of the pediatrician was of paramount importance. The danger of referring all behavior problems and difficulties to the clinical psychologist as an easy way for the pediatrician to sidestep his problems was brought out in the discussion.

Dr. Beverly brought up and discussed the difficult problem of the child who had the physical development of the fourteen-year-old, the mental development of the twelve-year-old, and with this the emotional control of a still younger child. The Chairman felt there was little value in trying to hasten puberty by hormones unless there was definite endocrine disturbance. It was pointed out by Dr. Charles Schott (Chicago) that it is best to widen out the activities of the child with superior intelligence and keep him with his physical age group. The question of "emotional maturity" in this connection was discussed by Dr. Schwab, Dr. Beverly, and the Chairman.

Health Education—Sex Education.—The point was stressed by the Chairman that health education before puberty was chiefly the formation of routine health habits. In early adolescence more formalized instruction in hygiene was possible. Sex education should not be overstressed but should fit into this course in hygiene. Dr. Schwab, Dr. Oliver Hill (Knoxville), Dr. G. F. Munns, Dr. S. J. Crumbine (New York City), Dr. I. H. Trumpeer (Chicago), Dr. W. B. McIlwaine (Petersburg, Va.), Dr. C. Harvey (Pontiac, Mich.), Dr. C. Schott (Chicago), Dr. E. H. Schorer (Kansas City), and Dr. Beverly took part in a general discussion of sex education. Considerable difference of opinion developed as to the relative function of the parent and the school. There was general agreement as to the danger of overemphasis of sex education by propagandists.

Overstrain and Physical Breakdown.—The question was raised as to the cause of the frequent breakdowns during adolescence. The Chairman stated he considered the complexity of modern life to be the chief factor. Individuals who lacked stamina on a constitutional basis tried to carry too heavy a load. Dr. Harvey stressed the educational problem with the college demands, as a most important factor. Dr. G. M. Lyon (Huntington, W. Va.) and Dr. Schwab emphasized the factor of parents

setting too high goals for many children, which made unreasonable demands upon them. There was need for a much sharper differentiation of adolescents who were attempting to enter on professional careers. Dr. Forbes (Denver) and Dr. E. T. McEnery (Chicago) discussed the importance and frequency of tuberculosis as a cause of the breakdown at this period.

Physical Exercise and Athletics.—Dr. Alvah Newcomb raised the question of the dangers of overexercise and certain sports to the child of this period. The Chairman stated that he felt that this was one of the most important points to be considered and referred to the dangers of excessive competitive exercise. Frequently the importance of the school team was placed before the welfare of the individual boy. Too much competitive sport with continuous training was bad. He considered that there was decided need for better medical supervision of athletics in the schools and referred to the frequency with which the boy needing exercise and athletics was put to one side while the natural athlete was given the entire supervision and training. Dr. Lyon spoke in particular of the dangers of basket ball. He referred to the tournaments held by the colleges for preparatory and high school boys in which four or five competitive games were played in the course of two or three days. Usually there is no medical supervision of such teams. Dr. Munns felt the track sports and basket ball were the most dangerous forms of adolescent sports unless they were most carefully supervised. Dr. Munns referred to the present attitude of many parents in recent years as being in agreement with the views being expressed at the Round Table. Dr. Oliver Hill (Knoxville) called attention to the danger of prohibiting sports and exercise to certain boys, as it made them stand out as exceptions and produced a bad psychologic effect upon the individual boy. Dr. Newcomb referred to the work of the Boy Scouts which he felt was in need of very much medical supervision. Dr. Schwab spoke of the wrong selection of sports for boys. Some boys are forced by their coaches or schools to take part in games in which they are not interested or may even dislike. The Chairman spoke of the problem of the nonathletic boy who has a secret longing or desire to be an athlete and because of his physical inability or lack of aptitude takes a contemptuous attitude toward sport as a defensive mechanism.

NOTE: Owing to the informal nature of the discussion at this Round Table it was necessary either to publish the entire proceedings of the two conferences or briefly to abstract the points discussed in a very general way. As the first method would require some sixty printed pages, the second method was adopted.

CONFERENCE OF REGION I OF THE AMERICAN ACADEMY OF PEDIATRICS AND THE TRI-CITY PEDIATRIC GROUPS

Region I of the Academy and the Tri-City Pediatric Groups (the New England Pediatric Society, Philadelphia Pediatric Society, and the Section of Pediatrics of the New York Academy of Medicine) met in a joint conference Oct. 19 and 20, 1934, at the New York Hospital—Cornell Medical Centre—and the Ambassador Hotel, New York City.

REPORT OF REGION I

December 1, 1934.

To the Executive Committee of the Academy of Pediatrics:

The Chairman of Region I begs leave to submit the following report of this date, covering the period since June of this year:

The membership of Region I, which now includes the eastern provinces of Canada, now totals 236.

For purposes of record it is to be noted that Dr. Edmund R. McCluskey has been appointed cochairman for Pennsylvania, Dr. Edward J. Wynkoop, cochairman for New York, Dr. William P. Buffum has succeeded Dr. Henry E. Utter as chairman for Rhode Island; and Dr. Alton Goldbloom has been appointed chairman for the eastern provinces of Canada.

The first regional conference was held in New York City on October 19 and 20. A program was carried out and is believed to be the precursor of an annual series which will stimulate interest in the Academy and prove an excellent means of getting the members together.

Between sessions a special meeting of the combined regional committeemen and the state chairmen was held with President Cooley and Dr. Grulee as guests.

Dr. Grulee opened the meeting with a discussion of the plans being made for the national meeting which is to be held in New York City next spring. He asked the active interest and support of all members in the East, spoke of the desirability of continuing Panel and Round Table Discussions, and outlined the plans for the meeting in their tentative form.

Maine.—Dr. Foster spoke of the difficulties of having a broad state program in the less densely populated states where so few men in the state were members and said he felt it would be desirable to have more explicit knowledge of what the Academy felt was a sensible program for such a state as Maine.

Dr. Grulee in discussion said that the first thing every Academy member should ask himself was, "How can I help?" He then spoke at some length of how different states had carried on activities, illustrating his point by examples of what has been done in certain states, and advised a careful reading of all reports of Academy activities in the JOURNAL OF PEDIATRICS.

Vermont.—Dr. Johnson reported that there had been an increased interest developed in diphtheria immunization and suggested that the Academy should take a much more active interest in the matter of radio advertisements concerning the welfare of children, as not infrequently the advertisements overstepped the bounds of truth.

New York.—Dr. Laws expressed the belief that each state must necessarily encounter different problems and that in the southern end of New York it is hoped

to place Academy men in positions of responsibility, whether in local pediatric societies or child welfare movements.

Maryland.—Dr. Smith spoke of certain difficulties in solidifying the work of the Academy. He felt confident that there will be a steady and sure growth.

New Jersey.—Dr. Nichols reported that many ways of putting Academy members to work have been found. A continued drive for diphtheria immunizations is still on; an attempt to secure more Mantoux tests is being evolved, the supervision of various programs of child welfare agencies is offered; a program of postgraduate teaching for general practitioners continues; and a program for the location of malnourished and neglected children has started with the objective of having a larger participation by both general practitioners and pediatricians. A gratifying increase in the membership in New Jersey was also noted.

Delaware.—Dr. Handy said that an attempt to secure better cooperation between agencies interested in the welfare of children was under way.

Connecticut.—Dr. Dunham said that there had been several meetings in which the importance of the Academy to the pediatricians of the state was emphasized.

Pennsylvania.—Dr. Stokes reported that the Academy members were taking an increased interest in all the problems concerned with children. There is still a great need for more education for physicians in the rural districts, and plans were being made to make this possible.

Quebec.—Dr. Goldbloom spoke of the many difficulties inherent in the pediatric situation. The chief of these is the division of the population into two distinct groups, French, and English. Not only is there no association between the ordinary population, but the medical groups themselves are as far apart as though they lived in different countries.

Rhode Island.—Dr. Buffum reported that the activities of the members have been in association with other pediatrists; as a result of this there has been a clearer understanding of what should be attempted. One outcome has been that all children entering school for the first time were examined, one-third of whom were examined by their own physicians.

The next business discussed was the meeting place for the Regional Conference next year. Philadelphia was chosen, the time to be decided by the Philadelphia group. The type of program was considered at some length, but no final decision was reached, it being felt that this should be left to the local committee.

The only recommendations that the Regional Committee makes to the Executive Committee are: first, that the wisdom of putting stars before the founders' names in the roster of members is questioned, and, second, that the Pennsylvania members do not believe that it will be wise to increase the dues at present.

The Chairman of Region I believes that there has been a steady growth of interest in the Academy in the East. This has been evidenced by many more applications for memberships, many more inquiries, and an attendance at the regional conference in New York City far exceeding anything that was expected. This increase in interest makes it very evident that along certain lines the Academy must plan much more definitely to define its work rather than to amplify it. It is believed that it is the part of wisdom to advocate the following proceedings:

1. It shall be required that all state chairmen report each year to the Regional Chairman on a blank to be drawn up by the Executive Committee.

2. Each state shall be required to have at least one yearly meeting which could easily be arranged to take place at the state society meeting. This is now voluntary but should be made obligatory.

3. The regional committeemen shall be asked to widen their activities beyond the mere supervision of application blanks. Each regional committeeman might be made responsible for the activities of the Academy in two or more states, both by conference with the state chairmen and attendance at various state meetings or conferences. In all cases in which objections are made to candidates, the regional committeeman for the district in which the question arises shall be asked to render a decision rather than the regional chairman.

4. It is believed to be a good policy to ask the Executive Secretary to furnish the Children's Bureau in Washington with a list of the members of the Academy and to request that all publications of the Bureau be sent to the members. This list should be kept up to date.

It is with regret that I announce the resignation of Dr. Ethel Dunham as chairman for Connecticut.

Respectfully submitted,

LOUIS C. SCHROEDER, M.D.

The program included the following papers, the abstracts of some of which are given:

October 19 at the Ambassador Hotel

Hypoparathyroidism. Arthur F. Anderson, M.D.

A diagnosis of hypoparathyroidism was made in this case because of the symptoms of stiffness of the extremities, increasing restlessness, persistent vomiting and headache, with the finding of a low blood calcium. The patient was a nine-year-old female white child. After the administration of parathyroid hormone, the calcium values in the blood rose, and the symptoms disappeared. She also received viosterol and thyroid extract.

Hyperteleorism. Louis Weymuller, M.D.

A white male child, nine years old, was presented as a case of hyperteleorism. The skull was wide laterally and flat in the occiput, the vault of the head being enlarged considerably beyond normal size. There was a large, high forehead with prominent frontal eminences. The eyes showed the usual appearance. The condition is essentially a developmental anomaly of the sphenoid bone of which there is an excessive growth of the lesser wings.

Third Ventriculoscopy as the Rational Treatment of Obstructive Hydrocephalus. John E. Scarff, M.D.

In this child who presented an extremely advanced case of hydrocephalus, the process seems to have been arrested by a procedure which carries with it a very low surgical mortality. It is unfortunate that the disease was so far advanced when the child was operated upon, but there is reason to believe that a similar procedure carried out in earlier cases could save many children for a useful and normal existence.

The treatment of nonobstructive (or communicating) hydrocephalus by the "closed" method, cauterization of the choroid plexuses through a "ventriculoscope" without removal of the cerebrospinal fluid, offers a much better prognosis than the original "open" method of operation on the plexus.

A new ventriculoscope is here described especially designed to allow exploratory and operative procedures to be carried out in the ventricles without removal of cerebrospinal fluid.

A case of nonobstructive hydrocephalus successfully operated upon with this instrument is here reported.

Birth Trauma. William E. Studdiford, M.D.

The anatomic relations in the head in the newborn infant, and the forces which come into play during labor and their after-effects are described. Emphasis is placed on the injuries which occur in the spine and the abdominal viscera especially the liver and adrenal gland.

It is pointed out that the greatest means of lessening the fetal and neonatal death rate in this group of cases lie along the lines of prevention.

The Acquisition of Language. Samuel T. Orton, M.D.

Report of Four Cases of Hirschsprung's Disease in Which the Presacral Nerve Was Resected. E. J. Donovan, M.D.

Four cases of Hirschsprung's disease are reported, in which resection of the presacral and inferior mesenteric nerves gave very satisfactory results. All the patients had spontaneous bowel movements before leaving the hospital and have had most satisfactory results from one to three years after operation.

Erythroblastic Anemia. Adolph G. DeSanctis, M.D.

Two cases of erythroblastic anemia occurring in young children of Greek and Italian families with the clinical findings and the course of the patients are described.

An Unusual Case of Glomerular Nephritis With Uremia. Roger H. Dennett, M.D.

To be published in a later issue of the JOURNAL OF PEDIATRICS.

The Treatment of Bronchiectasis in Children. John V. Bohrer, M.D.

All palliative treatments must be definitely limited in the length of time they are used in the group of patients in whom the disease is amenable to curative treatment.

Thoracoplasty and phrenicectomy are limited in their usefulness.

Bronchoscopic drainage is classified as only a palliative form of treatment.

Lobectomy is at present the only curative treatment. It still has too great a mortality, but with modern technic and teamwork this will be reduced.

The Treatment of Scurvy With Ascorbic Acid. Elvira Goettsch, M.D.

Three patients with infantile scurvy admitted to Babies Hospital were treated with ascorbic acid long enough for comparison with controls receiving equivalent amounts of orange juice. Serial roentgenograms were taken in an attempt to study healing of the subperiosteal lesions.

Clinical improvement was satisfactory in all the patients treated with ascorbic acid and was as effective as treatment with orange juice. Apparently pain was not relieved immediately by intravenous injection, but this was difficult to evaluate in apprehensive infants. Calcification of subperiosteal hemorrhages, as judged

by roentgenographic examination, appeared at an earlier date in those patients receiving ascorbic acid. Ascorbic acid may be given intravenously to infants without untoward effect in doses as high as 400 mg.

Urology in Pediatrics. Joseph F. McCarthy, M.D.

Vaccination in Anterior Poliomyelitis. John A. Kolmer, M.D., Philadelphia, Pa.

Congenital Air Cyst of the Lung. Harry S. Altman, M.D.

The following symptoms should lead one to suspect congenital cystic disease of the lung: unexplained attacks of dyspnea and cyanosis with signs of pneumothorax, especially when the past history discloses recurrent periods of labored breathing and when there is no evidence of any pulmonary infection or trauma. X-ray pictures generally show a lowering of the diaphragm on the affected side, a displacement of the mediastinum toward the opposite side, and the encapsulated air cavities.

Ophthalmoscopic Appearance of the Nerve Head in the Newborn. Samuel Karelitz, M.D.

Chronic Pulmonary Infiltration, Probably Lipoid Cell Pneumonia. B. S. Denzer, M.D.

The history and clinical findings are described. It is pointed out that the diagnosis is difficult. The relationship of lipoid pneumonia to nutritional disturbances is discussed.

Localized Tuberculous Meningitis. J. Brem, M.D.

A thirteen-month-old white female patient was admitted with a mass in the occipital region. Mucopurulent material which showed small collections of acid-fast bacilli was obtained. Inoculation into a guinea pig proved to be tubercle bacilli. Inoculation of spinal fluid also produced tuberculosis in a guinea pig. Tuberculin reactions in the patient were negative.

Refractory Rickets. D. V. McCune, M.D.

It is a well-known fact that the same quantity of vitamin D does not serve to protect all infants equally well against rickets. In some cases it is necessary to employ more than the ordinarily recommended doses of cod liver oil in order to insure proper growth of bone. In these individuals rickets is said to be refractory to the conventional modes of prevention and treatment.

In considering the etiology of rickets in this instance, heredofamilial factors were excluded. The diet was adequate in the ordinary sense of the word. The renal function was normal. Biologic studies showed that the child was able to absorb vitamin D from the alimentary tract in a normal manner. Chemical measurements of the metabolic balance of calcium, phosphorus, and magnesium served to exclude both hyperparathyroidism and also acidosis of degree sufficient to produce severe rickets.

A satisfactory explanation for the phenomenon could not be offered. Similar cases have been reported by Park, Blackfan, Freudenberg, and others. The case was placed in the category of refractory rickets. This designation is descriptive rather than explanatory. In the patient reported, healing was promoted by mas-

sive doses of viosterol. This fact suggested that the physiologic constitution of some individuals is such that although they ingest and absorb ordinary amounts of vitamin D, they still suffer from a relative deficiency of the vitamin.

Cretinism. Edward S. Rimer, M.D.

The child was a typical cretin who had gone untreated until the age of eleven years. She was the size of an infant of about two years and of a mental age of about four months. The prognosis for any considerable improvement at this late stage is poor.

Persistent Auricular Fibrillation. Lucy P. Sutton, M.D.

The patient was under observation from May, 1930, when he was five years old, up to the present time, when he is nine years and nine months old. The auricular fibrillation has persisted for three years and three months. There were no rheumatic manifestations.

Healing of Lung Abscesses. Edith M. Lincoln, M.D., and Antoinnette Raia, M.D.

Hereditary Hemophilia Treated With Theelin. Marshall C. Pease, M.D.

October 20 at the New York Hospital

Immune Reactions Induced in Infants by the Intestinal Absorption of Antigenic Protein. Oscar M. Schloss, M.D.

Studies on the Immune Response to Beta Hemolytic Streptococcus Infections. Vernon Lippard, M.D., and P. A. Johnson, M.D.

The Rôle of the Mantoux Test in the Diagnosis of Tuberculosis in Children. Hugh Chaplin, M.D.

The first part of the paper consists of a detailed description of a very carefully planned nursing and health service for a district of New York City having a population of 60,000. Included in the routine procedure is the Mantoux testing of each child at two years of age and yearly from then on as long as the test remains negative. In all positive cases roentgenograms of the chest are made, and the child receives the examination and recommendations of an expert in childhood tuberculosis. The known contacts of children with x-ray indication of tuberculosis are carefully investigated for any evidence of tuberculous infection.

Of those receiving one Mantoux test 6.8 per cent were positive. Among 240 of the children negative the first year who received a second yearly test, fourteen were positive, i.e., had been infected during the previous year.

Twenty-seven per cent of the children who were Mantoux-positive at the initial test showed x-ray evidence of tuberculosis, while only 10 per cent of those Mantoux-positive at the second yearly testing.

Three public health procedures are generally used for the diagnosis of tuberculosis in childhood: mass making of chest x-ray pictures of school children; following up known contacts of active cases followed in tuberculosis clinics; and routine Mantoux testing of all children beginning at an early age. The last two are the most useful. If they could be combined within one efficient public health organization, much would be accomplished toward the eventual elimination of tuberculosis in childhood.

Cases of Leukemia With Onset Simulating Rheumatic Fever. Carl H. Smith, M.D.

A Case of Rheumatic Fever Treated by Induced Fever. Katharine Dodge, M.D.

Roentgenologic Evidence of Cardiac Abnormality. May G. Wilson, M.D.

Lipoid Pneumonia. Charles Hendee Smith, M.D.

Experiences With Culture Grown Smallpox Vaccine. T. Campbell Goodwin, M.D.

Suppurative Pericarditis With Bilateral Empyema, Miner C. Hill, M.D.

Observations on the Utilization of Parenteral Fat. Harry Gordon, M.D.

Empyema With Gelatinous Exudate. DeWitt Hendee Smith, M.D.

A case of fibrinous empyema following serum-treated lobar pneumonia due to pneumococcus Type I is presented.

That the exudate was at first fibrinous with later liquefaction was substantiated by early failure to obtain pus on thoracentesis by aspiration of a plug of fibrin, by two injected air bubbles observed by roentgenograms suggesting that the bubbles were imbedded in a semisolid medium. At operation a central core of undissolved fibrin was found.

The injection of air in this case gave data of primary importance in understanding the pathology.

Chronic Ulcerative Collitis With Peritonitis Following Perforation. William C. Anderson, M.D.

Tissue Response of White and Colored Children to Induced Tuberculosis. Milton I. Levine, M.D., and W. H. Park, M.D.

An Epidemic of Pneumococcus (Type I) Infection. Parker Dooley, M.D.

Torsion of the Omentum. John W. Buckley, M.D.

At operation, the right half of the omentum was found to be the site of a torsion about an inch below its attachment to the hepatic flexure and the transverse colon. The symptoms were a sudden onset of colicky abdominal pain in the right lower quadrant which became progressively more severe. Vomiting occurred.

REPORT OF PEDIATRIC DEPARTMENTS IN GENERAL HOSPITALS

(Conclusion)

REPORT OF THE COMMITTEE ON HOSPITALS AND DISPENSARIES, AMERICAN ACADEMY OF PEDIATRICS

PREVIOUS reports have reviewed pertinent information concerning pediatric care among hospitals in each of the regions of the Academy of Pediatrics, which have twenty-four or more beds and bassinets exclusively for infants and children.

We here attempt to make a comparative and composite report formulated from the data given in the earlier reports.

TABLE I

NUMBER OF HOSPITALS

Region I	135
Region II	21
Region III	65
Region IV	14
Total	235

According to the 1934 report of the American Medical Association, there are in this country 6,437 hospitals. Among this number probably about 4,000 can be strictly designated as general hospitals, and about 5.8 per cent of all general hospitals have pediatric services of sufficient size to be eligible for consideration in our report. According to the report of the Committee on Medical Care for Children of the White House Conference, more than half of the general hospitals have capacities of less than fifty beds, and 75 per cent of them have less than one hundred beds. These figures may help explain the reason why only 5.8 per cent of the general hospitals have twenty-four or more beds and bassinets for children.

When we examine the data for the separate regions in Table I, we find that Region I has more than twice as many qualified services as the next highest region, which is Region III, six times as many as Region II, and almost ten times as many as Region IV. Population figures explain these differences only partially. When we consider census reports for the four regions, we find that they are, according to last census, 1930, as given in Table II.

TABLE II

REGION I	REGION II	REGION III	REGION IV
12 eastern states	14 southern states	13 midwest and	10 far western
36,765,866	35,499,838	western states	states
		39,527,891	10,860,431

Population is apportioned over vastly greater areas in Regions II, III, and IV, and, of course, there are relatively fewer cities in these areas than in Region I. Thus, if all other factors are the same, the size of the hospitals would be expected in general to be smaller in the latter three regions. Small communities usually do not have large hospitals, and children's services of twenty-four or more beds usually

are found only among the larger hospitals. Other factors of importance are the relative wealth of the respective regions and the greater number of medical centers such as medical schools and clinics, to be found in Regions I and III. Region IV, for instance, includes a large part of this country but possesses a population of less than one-third that of either of the other three regions. In eight states of Region IV there are no hospitals having pediatric services of the size considered here, and of the total of fourteen with services found in that region twelve are in California.

TABLE III

BEDS		BASSINETS	
Region I	6835	Region I	5749
Region II	1162	Region II	601
Region III	2707	Region III	1697
Region IV	878	Region IV	505
Total	11,582	*Total*	8552

The White House Conference report lists about 39,837 beds for children among 4,021 general hospitals. Hospitals reported here then have about 29 per cent of this total number.

TABLE IV

TOTAL ADMISSIONS (1933)

CHILDREN		NEWBORN	
Region I	116,723	Region I	99,805
Region II	26,675	Region II	14,512
Region III	45,252	Region III	34,745
Region IV	10,425	Region IV	9,355
Total	189,075	*Total*	158,417

An interesting point concerning these figures is that total newborn admissions almost equal total children's admissions among these hospitals.

This fact makes the newborn departments of relatively great importance.

TABLE V

ATTENDING STAFF (PEDIATRISTS)

Region I	540	
Region II	85	
Region III	295	100 per cent of the hospitals have a special pediatric attending staff.
Region IV	96	
Total	1016	

About one-fourth of the total number of physicians especially interested in pediatrics in this country are members of the attending staffs of these hospitals.

TABLE VI

NEWBORN SERVICE UNDER SUPERVISION OF PEDIATRIC DEPARTMENT

Region I	67	50%
Region II	14	66%
Region III	31	47%
Region IV	8	57%
Total	120	51%

Among 1,403 general hospitals replying to a questionnaire sent out by the White House Conference Committee only 56 per cent had a special attending staff for the pediatric department.

Among 806 replies to the White House Conference questionnaire 14.8 per cent reported pediatrists in charge of newborn services.

TABLE VII

HOSPITALS HAVING RESIDENTS WHOSE TIME IS EMPLOYED PART OR EXCLUSIVELY ON THE PEDIATRIC SERVICE

Region I	33
Region II	10
Region III	15
Region IV	10
Total	68

Eighty-five residents are employed among the sixty-eight hospitals, and of these fifty-six, or 65 per cent, are employed exclusively in the pediatric department.

TABLE VIII

HOSPITALS HAVING INTERNES WHOSE TIME IS EXCLUSIVELY EMPLOYED IN THE PEDIATRIC DEPARTMENT

Region I	30	22%
Region II	4	19%
Region III	6	9%
Region IV	3	21%
Total	43	18%

TABLE IX

HOSPITALS IN WHICH THE HEAD NURSE IN CHARGE OF THE PEDIATRIC DEPARTMENT HAS HAD SPECIAL PEDIATRIC TRAINING

Region I	121	90%
Region II	15	71%
Region III	62	95%
Region IV	12	89%
Total	210	89%

TABLE X

HEAD NURSES WITH SPECIAL PEDIATRIC TRAINING LIMITED TO LESS THAN 6 MONTHS

Region I	28		15
Region II	4		5
Region III	9	No reply	12
Region IV	2		4
Total	43 (20%)		36 (17%)

Twenty per cent of the head nurses in charge of the pediatric departments have had less than six months of special pediatric training. The proportion may be still larger, as 17 per cent of the hospitals failed to answer this question.

TABLE XI

HOSPITALS HAVING SOCIAL SERVICE DEPARTMENTS AVAILABLE TO THE PEDIATRIC DEPARTMENT

Region I	56	41%
Region II	7	33%
Region III	20	30%
Region IV	5	36%
Total	88	

Thirty-seven per cent of all hospitals have social service departments available for use by the pediatric departments.

Among a total of 4,268 hospitals replying to the White House Conference questionnaire, only 9.84 per cent reported that they had a social service department.

TABLE XII

HOSPITALS HAVING A SPECIAL DIET KITCHEN

	FOR INFANTS		FOR CHILDREN	
Region I	125	92%	65	48%
Region II	14	69%	11	52%
Region III	50	77%	29	44%
Region IV	10	71%	6	43%
Total	199		111	

Eighty-four per cent of all hospitals have special diet kitchens for infants, and 47 per cent have them for children.

TABLE XIII

HOSPITALS SUPPLYING SCHOOLING AND RECREATION FOR CONVALESCENTS

	SCHOOLING		RECREATION	
Region I	46	34%	93	68%
Region II	4	19%	5	24%
Region III	20	30%	30	46%
Region IV	5	35%	6	43%
Total	75		134	

Thirty-one per cent of all hospitals provide schooling, and 57 per cent provide recreation for convalescents.

Seventy-seven per cent of all hospitals have a children's dispensary.

TABLE XIV

HOSPITALS HAVING A SPECIAL DISPENSARY FOR CHILDREN

Region I	113	83%
Region II	19	90%
Region III	40	61%
Region IV	11	80%
Total	183	

TABLE XV

HOSPITALS IN WHICH THE SAME STAFF SERVES IN BOTH HOSPITAL AND DISPENSARY

Region I	104	79%
Region II	14	69%
Region III	37	55%
Region IV	10	71%
Total	165	

In 70 per cent of all hospitals the same staff serves both hospitals and dispensary.

TABLE XVI

HOSPITALS IN WHICH RESIDENTS AND INTERNES HAVE DUTIES IN THE PEDIATRIC DISPENSARY

	RESIDENTS		INTERNES	
Region I	24	72%	85	62%
Region II	6	60%	13	61%
Region III	13	87%	31	47%
Region IV	7	70%	9	64%
Total	50		138	

Among sixty-eight hospitals employing pediatric residents, 73 per cent afford the resident dispensary duties, and 58 per cent of the internes in all of the hospitals have duties in the pediatric dispensary.

TABLE XVII

PERCENTAGE OF CHILDREN'S DEATHS AND NECROPSIES

	DEATHS	NECROPSIES
Region I	4.3 %	39.2%
Region II	6.1 %	21.7%
Region III	4.2 %	43.7%
Region IV	7.07%*	27.0%*
General average for children's deaths		5.4%
General average for children's necropsies		32.4%

*One state gave no reply.

TABLE XVIII

PERCENTAGE OF NEWBORN DEATHS AND NECROPSIES

	DEATHS	NECROPSIES
Region I	2.9%	39.5%
Region II	5.1%	20.2%
Region III	4.1%	37.7%
Region IV	3.6%*	36.0%*
General average for newborn deaths		3.9%
General average for newborn necropsies		33.3%

*One state gave no reply.

COMMENTS AND CONCLUSIONS

Regions I, II, and III have about the same population yet there is a marked difference in the number of qualified pediatric services in the respective regions. Apparent reasons for this difference have been given. The same explanation may be

given for Region IV, plus the fact that the total population of that area is less than one-third that of each of the first three regions.

The 1934 report of the American Medical Association lists a total of 1,027,046 beds and 52,464 bassinets among 6,437 hospitals in this country. The hospitals considered in this report reserve about 1 per cent of that total number of beds for children but more than 15 per cent of that number of bassinets. As has been previously stated, questionnaires returned from 4,021 general hospitals revealed that there were available only about 39,837 beds for children, some of these not necessarily restricted to use by children. Hospitals considered in our reports have about 29 per cent of this total number.

Among a part of 1,403 general hospitals replying to the White House Conference questionnaire, there was an average of about eight beds per hospital for babies and about twelve beds for children from two to four years old. The average number of beds for children among hospitals considered in our report is forty-nine, bassinets, 36. These figures indicate rather clearly that most of these 235 hospitals are fairly large general hospitals. Their total number of children's admissions for 1933 is better than 33 per cent of the total number of children's admissions to the 1,403 general hospitals of the 1929 White House Conference report.

Figures on newborn infants for the year 1933 also indicate that in general the obstetric departments of these general hospitals are large. The relative importance of the newborn departments becomes more apparent when we find newborn admissions almost equaling the children's admissions. In view of the fact that newborn departments in these hospitals are comparatively large, care and supervision in them should be as efficient as possible. Probably the most effective care of the newborn is secured when that department is under the supervision of the pediatric department. However, only 51 per cent of the hospitals have pediatric supervision of the newborn department. The highest percentage of such care occurs in Region II, the lowest, in Region III. When one compares this figure of 51 per cent to the 14.8 per cent for pediatric department supervision reported among 806 hospitals in the White House Conference report, the former figure is favorable. However, 100 per cent of the hospitals considered in this report have a special pediatric attending staff. When one examines the newborn death rate percentages for each region and particularly for individual hospitals, it becomes apparent that many departments cannot be very proud of their newborn mortality records. Pediatric supervision of newborn departments has provided favorable results in practically all instances in which it has been adopted. There are none of these hospitals which lack a pediatric staff. There must be, at most, few in which that staff could not or should not supervise the newborn department.

Data concerning pediatric internes and residents need little additional discussion except to say that about 25 per cent of the hospitals have pediatric services of sufficient size to warrant a pediatric resident and that about 65 per cent of these residents are employed full time on that service.

Head nurses in charge of a specific department, if they are to be particularly efficient in their work, should have special training in that specialty. Eleven per cent of the hospitals report that their head pediatric nurses have not had special pediatric training. Twenty per cent of those who had special training have had less than six months of it; 17 per cent did not reply, and probably a large percentage of this number should be added to the 20 per cent. The committee feels that head nurses in charge of pediatric departments should have at least six months of special pediatric training and preferably one year in that specialty.

Too few hospitals have social service departments for, or available to, the pediatric department. Certainly children's services of the size considered here must meet a

considerable number of problems in which the cooperation of a social service department would be helpful and at times almost indispensable. This is again a serious weakness among these hospitals.

We were pleasantly surprised to observe the number of hospitals which have a special diet kitchen for children, but we feel that all of them should have special diet kitchens or milk laboratories for infants. Sixteen per cent of the hospitals do not have them.

Schooling for convalescents is provided in fewer than one-third of the hospitals (31 per cent) and in as few as 19 per cent in Region II. Many of these hospitals probably have comparatively few children of school age confined for long periods of convalescence. Schooling may not be of particular importance in these instances although it should be provided in every hospital in which there are a number of convalescents.

Recreation for convalescents should also be available in each hospital. Fifty-seven per cent of the hospitals report that they provide for it.

A large proportion (77 per cent) of the hospitals report that they have special pediatric out-patient dispensaries, and among about 70 per cent of these the dispensary and hospital have interlocking staffs. A majority of these dispensaries are open three days each week, and those of the larger hospitals are open daily. Average dispensary attendance appears to be about twenty to thirty patients. If we allow an average of twenty-five patients per dispensary with the dispensary open only three days weekly, it would mean that there are about 1,000,000 visits yearly. However, many of these children's dispensaries are open daily, which would mean that as near as we can estimate there are probably at least between one and one and one-half million visits yearly to the pediatric out-patient departments of 235 general hospitals. One and one-half millions more or less of dispensary visits each year would suggest that the pediatric out-patient departments of general hospitals can, and probably do, play an important rôle in child health problems throughout the country.

Seventy-three per cent of pediatric residents and 58 per cent of the pediatric internes have duties in the dispensary. Unquestionably such duties enhance the value of a residency or interneship, and it is advisable that dispensary experience in pediatrics be made available to all residents and internes who desire such pediatric experience.

Death rates may be misleading if they are used as a gauge of hospital efficiency, although newborn death rates we believe are an important index of the efficiency of respective obstetric and pediatric departments, and particularly the efficiency of their cooperation. Region I can boast of the lowest figure in this respect.

Necropsy figures are particularly apt to reflect the spirit of serious research and scientific, efficient medical care associated with an institution. The average newborn and children's necropsy incidence for the four regions is 33 per cent, about 8 per cent higher than that reported among 1,002 hospitals replying in 1929 to the White House Conference questionnaire, but this is only about half of the percentage achieved by children's hospitals in this country. Region II makes a rather poor showing in this respect; this figure combined with their high children's and newborn death rate figures suggests that pediatrists and obstetricians in that area have a worth-while problem to solve.

It is to be hoped that newborn and children's death rates may be lowered and necropsy percentages bettered in all regions.

Academy News

The American Academy of Pediatrics will hold its fifth annual meeting at the Waldorf-Astoria Hotel in New York City on June 7 and 8, 1935. There will be four panel discussions on the following subjects: "Chronic Pyuria and Its Surgical Indications," under the direction of Dr. Hugh Cabot; "Prevention of Colds in Children," under the direction of Dr. L. W. Dean; "The Pituitary Gland," under the direction of Dr. R. G. Hoskins; and "Vitamin D," under the direction of Dr. E. V. McCollum. There will also be a number of round table discussions and a general meeting. It is expected that there will be a large attendance at this meeting. It will precede the meeting of the American Medical Association in Atlantic City, June 10 to 14.

News and Notes

On March 6, under the direction of Dr. Morgan Smith, of Little Rock, with the blessing of Dr. E. C. Mitchell, of Memphis, Tenn., the Arkansas State Pediatric Association was launched.

Dr. Adolph G. DeSanctis has been appointed Director of the Department of Pediatrics of the New York Post Graduate Medical School and Hospital, Columbia University.

Dr. H. E. Coe has been chosen Chief of Staff and Dr. J. I. Durand, Chief of the Pediatric Department of the Children's Orthopedic Hospital in Seattle.

At the meeting of the American Pediatric Society in Cleveland on May 2, 3, and 4, Dr. Fritz B. Talbot, Boston, was elected president; Dr. Franklin P. Gengenbach, Denver, vice-president; Dr. Hugh McCulloch, St. Louis, secretary and treasurer; and Dr. Heyworth N. Sanford, Chicago, recorder-editor for the ensuing year.

Professor A. J. Carlson of Chicago was a guest of the Society at the meeting.

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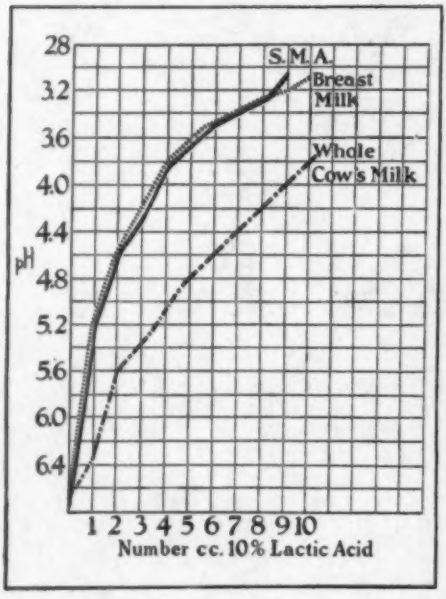
In BUFFER VALUE *too*, S.M.A. *resembles* BREAST MILK



This buffer chart shows the close similarity between the buffer value of S.M.A. and Breast Milk and the wide difference between cows' milk and Breast Milk. ***This also explains why it is not necessary to add an acid to S. M. A.***

Breast Milk from the Normal Mother is the Ideal Food for the Human Infant. That is why S.M.A. is made to resemble breast milk in percentages of carbohydrate, protein, fat and total salts (ash) content, and why even the chemical and physical constants of the fat in S.M.A. are like those of breast milk fat.

This photograph shows the equipment for determining hydrogen ion concentration necessary to plot the Buffer Curve. The chemist drops a measured quantity of acid (from the tall tube in the right foreground) into solution to be tested (in the beaker below) and records the readings from the dial before him.

S.M.A. is a food for infants—derived from tuberculin tested cows' milk, the fat of which is replaced by animal and vegetable fats including biologically tested cod liver oil; with the addition of milk sugar and potassium chloride; altogether forming an antirachitic food. When diluted according to directions, it is ***essentially similar to human milk*** **in percentages of protein, fat, carbohydrates and ash, in chemical constants of the fat and in physical properties.**

S. M. A. CORPORATION « ◎ » CLEVELAND, OHIO